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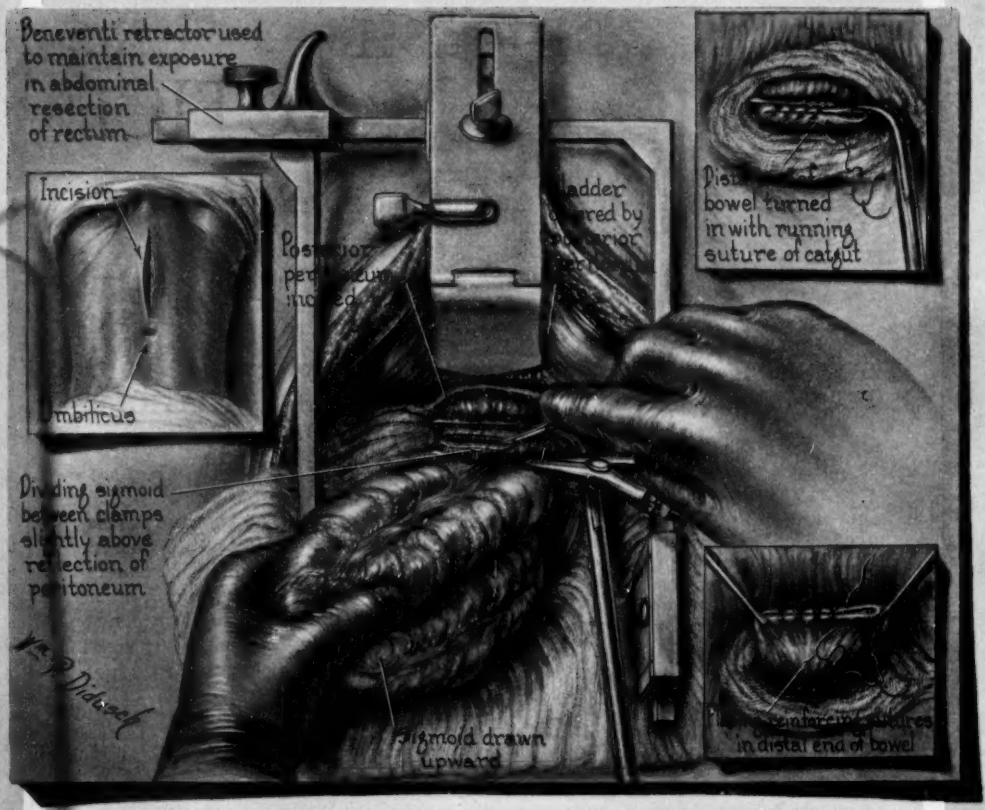
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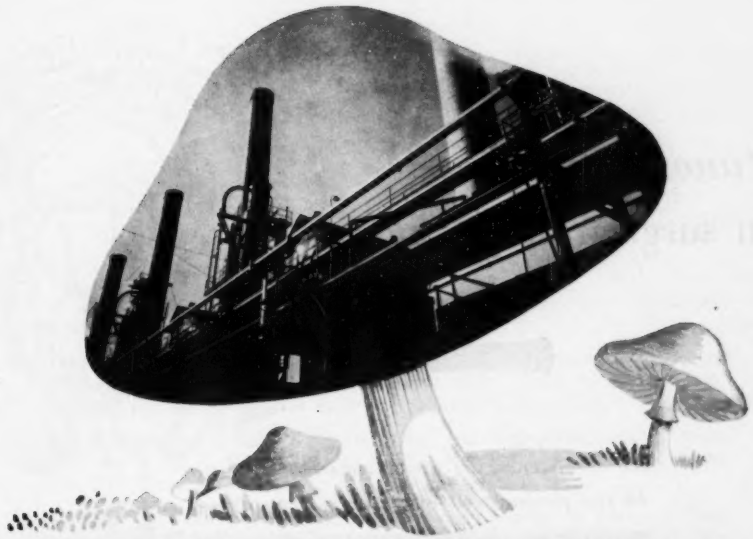

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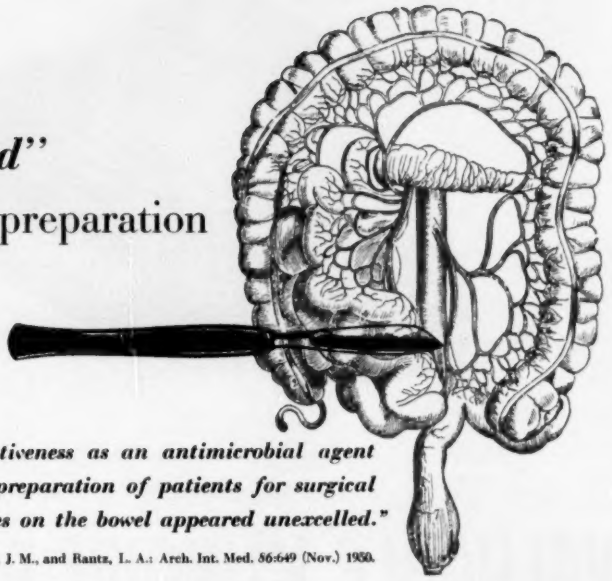

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Di Caprio, J. M., and Rantz, L. A.: Arch. Int. Med. 86:649 (Nov.) 1950.

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VOLUME 62 FEBRUARY 1951 NUMBER 2

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GASTRIC RESECTION IN THE TREATMENT OF PEPTIC ULCER

FRANK GLENN, M.D.
AND
CHARLES S. HARRISON, M.D.
NEW YORK

GREATER discretion is exercised today in the surgical treatment of peptic ulcer than at any former time. Rarely is surgical treatment employed before an adequate trial on an intelligent medical regimen has failed. Definitive therapeutic operations are fewer than in 1930 and are accomplished with low mortality and morbidity. Today, three operations are employed almost exclusively in the surgical treatment of peptic ulcer. They are gastric resection, gastroenterostomy and vagotomy. They are not new procedures. Each has been credited with successes, complications and failures that have been duly recorded in the medical literature over the past 50 years.

Twenty years ago the major American clinics appeared convinced that gastroenterostomy was the procedure of choice. A large number of papers from these clinics reported apparent success with this procedure in 80 to 85 per cent of the patients on whom it was used. Its operative mortality rate was low, much lower than that for gastric resection, and immediate resulting complications appeared to be few. Later follow-up studies [1] on these patients, however, revealed that short term observations of five years or less were inadequate. Longer studies revealed that although 50 per cent of the patients who showed recurrence of symptoms and complications requiring further surgical intervention did so within five years of their primary procedure and 90 per cent did so within 15 years there was no actual time lapse that precluded recurrence.

A few surgeons, such as A. A. Berg,[2] insisted as early as 1930 that gastric resection produced better results than gastroenterostomy. This contention was slow in being accepted, however, because of the high mortality rate then associated with the procedure and the fact that it was an operation of greater magnitude, but by 1940 the trend throughout the country favored gastric resection. As the operation increased in frequency, the mortality rate associated with it diminished, and longer periods of postoperative observation left little doubt as to the superiority of its results over those of gastroenterostomy.

From the Department of Surgery, the New York Hospital–Cornell Medical Center.

1. Priestly, J. T., and Gibson, R. H.: Gastrojejunal Ulcers: Clinical Features and Late Results, Arch. Surg. **56**:625 (May) 1948. Glenn, F.: Secondary Operations for Peptic Ulcer, Ann. Surg. **132**:702, 1950.

2. Berg, A. A.: The Mortality and Late Results of Subtotal Gastrectomy for the Radical Cure of Gastric and Duodenal Ulcer, Ann. Surg. **92**:340, 1930.

The evolution of the surgical treatment for peptic ulcer seemed now to have reached the stage where one procedure invariably would be employed unless there were contraindications to it. This was in contrast to the earlier days when numerous operations with many variations were tried. Then in 1943, Dragstedt [3] reported on two patients with peptic ulcer treated with vagotomy. Since that time it has been used alone or combined with gastroenterostomy in several thousand patients. Recent follow-up reports, however, indicate that vagotomy, either with or without gastroenterostomy, leaves much to be desired as a primary surgical procedure for peptic ulcer.

The scope of peptic ulcer includes duodenal, gastric and esophageal ulcers as primary lesions and marginal and jejunal ulcers as lesions secondary to operations done for the first. Medical treatment of primary lesions is commonly credited with success in 85 per cent of all patients with ulcer. Surgical treatment affords relief for all but 10 per cent of the remaining patients at the primary operation. This leaves an incidence of one tenth to one fifth of 1 per cent of all patients with ulcer who acquire marginal and jejunal ulcers. Of the patients requiring surgical intervention,

TABLE 1.—*Distribution of Lesions in 309 Patients Subjected to Gastric Resection*

Duodenal	206
Gastric	74
Gastric and duodenal	9
Marginal	19
Jejunocolic	1
	309

it represents 5 to 15 per cent. By comparison, it would seem that the surgical therapy directed toward the medical failures was good but could be improved on.

The Department of Surgery [4] at this center, along with many others in the country, formerly believed that gastroenterostomy promised the best results. During the past ten years, however, our observations have convinced us that gastric resection is a better procedure for peptic ulcer. Our experience with it over a four year period, from Jan. 1, 1946 to Dec. 31, 1949, is presented in order to evaluate the morbidity and mortality in the light of improved preoperative and postoperative care, better operative technic and antimicrobial therapy. It is hoped that other clinics will report their recent experience also, so that some of the controversial aspects of the surgical treatment of peptic ulcer may be resolved.

Three hundred and nine patients were subjected to gastric resection for peptic ulcer at the New York Hospital between Jan. 1, 1946 and Dec. 31, 1949. Their lesions were distributed as shown in table 1.

There were 243 men in the group (78.6 per cent) and 66 women (21.4 per cent). Their ages ranged from 20 to 85, with almost two thirds being in the 40 to 50 decade. Usually pain was the first symptom, occurring in 300 cases (97.1 per cent), followed by or associated with nausea and vomiting in 191 instances (61.8

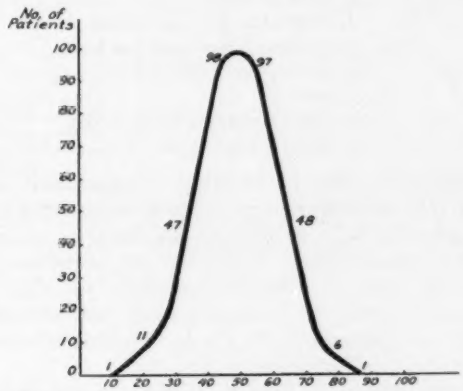
3. Dragstedt, L. R., and Owens, F. M.: Supra-Diaphragmatic Section of the Vagus Nerves in Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53**:152, 1943.

4. Cooper, W. A.: End Results in the Treatment of Peptic Ulcer by Posterior Gastroenterostomy, Surgery **23**:425, 1948.

per cent). Generally speaking, as these symptoms became intensified, other manifestations of ulcer, such as obstruction or bleeding, often appeared. Duration of symptoms averaged almost ten years for the group.

Sixty-seven patients in the group had undergone previous procedures for their ulcer, as given in table 2. Seventy-three patients (23.6 per cent) were considered to have complete or partial obstruction on the basis of clinical or roentgenologic findings; 24 in this group were found to have complete obstruction.

One hundred and forty-nine patients (48.5 per cent) were bleeding on their admission to the hospital or gave a history of bleeding at a prior time. This group had 297 recorded episodes of bleeding, 145 of which were considered to be minor episodes but 152 were considered as massive hemorrhage. Of the latter, 53 occurred on the patients' admission to our hospital. Our criteria for massive bleeding is a red blood cell count of 3,700,000 or less and associated signs of acute blood loss.



Age range of 309 patients subjected to gastric resection for peptic ulcer at the New York Hospital, 1946-1949.

TABLE 2.—*Primary Operations (Sixty-Seven) in 309 Patients Who Underwent Gastric Resection*

Procedure	No.
Plication for perforation	36
Gastroenterostomy	20
Vagotomy	6
Pyloroplasty	1
Gastric resection	1
Gastrostomy	1
Dismantling for fistula	1
Jejunal graft	1
	67

Ninety-five of the patients (30.7 per cent) had a guaiac-positive stool (plus 4) on their admission. Of the 53 who bled massively, all but 15 stopped bleeding on a conservative regimen. These 15, 28.3 per cent of the group with massive bleeding or 4.85 per cent of the group as a whole, were subjected to emergency gastric

resection. Two patients died postoperatively, a mortality rate of 13.3 per cent for the emergency procedures. The average age of the patients was 53.7 years. Eleven of the 15 with persistent bleeding were men, and four gave a history of previous bleeding. All the hemorrhages were from duodenal ulcers except two. One of these was from a marginal ulcer and the other from a gastric ulcer. Significant laboratory findings were the degree of acidity and the persistence of blood in the stools. Generally speaking, the patients showed a hyperacidity after a test meal ranging as high as 140. There were only a few with a normal or low acidity, and none had anacidity.

PREOPERATIVE PREPARATION

The method of preparation naturally varied with the patients and depended on their complaints when admitted. If the patient was thought to be actively bleeding, the following regimen was used:

1. Nothing by mouth
2. Fluids by clysis
3. Observation every 30 minutes
4. Morphine sulfate every four hours if respiratory rate over 14
5. Bed rest
6. Multiple small blood transfusions
7. Frequent blood counts

If the patient continued to bleed so that further exsanguination was not prevented by transfusion of 1,000 cc. of blood every 24 hours, the operating room was notified and the patient taken to the x-ray room for an emergency gastrointestinal study if the site of bleeding was obscure. From there the patient was taken directly to the operating room, where an emergency procedure was done. If he stopped bleeding, 30 cc. of milk and cream was given every hour in addition to antacids, phenobarbital and belladonna. The diet was then gradually advanced over a period of five or six days to a six feeding soft gastric diet.

If the patient was thought to have obstruction, a Levin tube was passed and gentle suction applied. This was continued until the amount of drainage indicated relief of the obstruction. During this period extreme care was taken to maintain the acid-base balance. The patient was then started on 30 cc. of milk and cream, with aspirations in the early morning and late evening. As evidence was accumulated that little, if any, obstruction remained, the diet was advanced and aspirations done only in the evening and eventually discontinued.

If the patient complained of pain, he was given 120 cc. of milk and cream every hour, water as he wished, antacids, phenobarbital and belladonna. If this regimen did not relieve the pain within a 24 hour period, a Levin tube was passed and continuous intragastric drip instituted. We used 300 cc. of milk and cream over a two hour period, followed by 300 cc. of amigen® over a similar length of time. These were alternated continuously day and night. All patients on whom this regimen was used responded well. After the patient was comfortable for 36 hours, the Levin tube was removed and the milk and cream regimen started again, with a gradual advancement of the diet.

In the preoperative work-up a gastric analysis with histamine was done with few exceptions. No correlation, however, could be established between the results of gastric analysis and either severity of symptoms or postoperative course.

ANESTHESIA

The choice of anesthesia was made with great care in each case, the age and general condition of the patient being taken into particular consideration. Nitrous oxide and ether were used oftener for the earlier cases in this series, but thiopental sodium (pentothal®) with cyclopropane and thiopental sodium with ether have become the commoner choices. Only once did cyclopropane cause such a pronounced cardiac irregularity that ether was substituted during the procedure. Intercostal blocks and local anesthesia were seldom used and then only for patients in the most severe preoperative state. It should be mentioned that all our patients who were given a general anesthesia had endotracheal intubation to prevent possible aspiration of regurgitated gastric content.

Two thirds of the patients, or 66.7 per cent, had duodenal ulcers, and 74, or 23.9 per cent, had gastric ulcers. Nine had double lesions, both gastric and duodenal, 19 had marginal ulcers and one had had a jejunal transplant. Every effort was made to remove the ulcer in each instance, but if at any time during the procedure

TABLE 3.—*Anesthesia Used in 309 Gastric Resections*

Nitrous oxide and ether	96
Thiopental sodium and cyclopropane	89
Thiopental sodium and ether	84
Nitrous oxide and cyclopropane	9
Cyclopropane	9
Ether	8
Thiopental sodium, cyclopropane and ether	4
Thiopental sodium, cyclopropane and spinal anesthesia	3
Intercostal block and thiopental sodium drip	2
Intercostal block and local anesthetic	2
Continuous spinal anesthesia	1
Local anesthetic and cyclopropane	1
Local anesthetic and ether	1
	309

the operator felt that further dissection in the region of the ulcer was hazardous or that closure of the duodenum would be jeopardized because of inflammatory reaction and proximity to the common bile duct, the ulcer was left undisturbed. Ulcers on the posterior wall of the duodenum often perforate into the pancreas and are associated with extensive reaction in the surrounding structures. Closure of such a duodenum may be followed by dehiscence, a complication which is as serious as the bleeding that may ensue if the ulcer is not removed.

As shown in table 4, several types of resection were used, but the Polya type was the most popular, being employed in 219 cases, or 71 per cent. The retrocolic Polya procedure was used in 117 cases. We were unable to correlate any significant difference between the period of follow-up and the type of procedure. At the present time, however, we believe that the Billroth II is not an adequate procedure, and we use the Polya or Hoffmeister method almost exclusively.

Of the 309 patients subjected to gastric resection, 94, or 30.4 per cent, had postoperative complications, fatal in 6 (1.9 per cent) and nonfatal in 88 (28.5 per cent). Two of the fatalities occurred after emergency procedures, reducing the elective mortality rate to 1.3 per cent. The 88 patients had a total of 96 nonfatal complications, six patients having multiple complications. One, for example, had

atelectasis in the lower lobe of the right lung, pneumonia in the upper lobe of the left lung and acute urinary retention. These were classified as three individual

TABLE 4.—*Types of Resection Used on 309 Patients with Peptic Ulcer*

Polya		
Posterior Polya	117	
Anterior Polya (1 with vagotomy)	92	
Dismantling with posterior Polya	5	
Dismantling with anterior Polya	5	
	219	
Hoffmeister		
Posterior Hoffmeister (1 with vagotomy)	24	
Anterior Hoffmeister (1 with vagotomy)	55	
Dismantling with posterior Hoffmeister	1	
Dismantling with anterior Hoffmeister	1	
	81	
Billroth II (2 with vagotomy)	8	
Esophagogastrostomy	1	
Total	309	

TABLE 5.—*Nonfatal Complications Following 309 Gastric Resections*

Wound (9)		
Infection	4	
Dehiscence	4	
Iodine burn	1	9
Gastrointestinal (53)		
Gastric retention	41	
Hemorrhage	6	
Paralytic ileus	3	
Leaking duodenal stump	3	53
Cardiorespiratory (26)		
Heart		
Heart failure	1	
Lungs		
Pneumonia	13	
Atelectasis	5	
Asthma	1	
Infarct		
With evidence of thrombophlebitis	5	
Without evidence of thrombophlebitis	1	26
Cerebrovascular (1)		
Thrombosis of anterior ventral artery		1
Extremities (2)		
Thrombophlebitis without pulmonary infarct		2
Genitourinary (4)		
Acute retention		4
General (1)		
Tetany due to hypocalcemia		1
Total nonfatal complications		96

complications. As can be seen from the ensuing table, 9 of the 96 complications involved the wound itself. Four of these were wound infections, while in four there was dehiscence. All the latter were closed with through and through silver wire sutures, and the patients recovered.

Of the 96 nonfatal complications, 53, or 55.2 per cent, were directly related to the procedure, excluding the wound complications. By far the greatest number of these, 41 in all, were concerned with postoperative gastric retention, or the so-called ninth day disease. A particular search was made in each case of gastric retention to try to throw some light on the cause of this common complication. The history, preoperative preparation, operative procedure and postoperative care of each patient were studied, but no common factor could be found. Perhaps the solution lies in the fluid balance, although this is but speculation. Only 3 of the 41 patients with gastric retention required surgical intervention; in these enteroenterostomy was done. One patient had retention for 31 days postoperatively, but it cleared up on conservative management, and he has now been asymptomatic for over two years. Six patients had gastrointestinal bleeding postoperatively. Bleeding occurred two to six days after operation but was never severe enough to cause a critical state in the patient. We believe that this complication arose from the anastomotic site, since only one of the six patients was operated on for a bleeding ulcer, which was removed at the time of operation. All were given blood transfusions and were successfully treated by conservative means.

Of the three cases in which complications were attributed to a leaking duodenal stump, drainage was carried out in only two, as the diagnosis was presumptive in the third. The patient in this last case had an elevated temperature and signs and symptoms suggestive of a questionable perforated duodenal stump, but these were never severe enough to warrant exploration. In the other two exploration and drainage were performed; all three patients recovered.

Twenty-six of the complications, 27.1 per cent, were related to the cardiorespiratory system. This is a reasonably small number inasmuch as 17.8 per cent of all the patients were over 60 years of age. We did not have a patient with postoperative coronary occlusion, but we did have one with heart failure that cleared when digitoxin was given. There were 18 instances of postoperative pneumonia and atelectasis. We believe that without adequate chemotherapy the rate would have been much higher. Of equal importance is the fact that all the patients were mobilized the day of operation. Furthermore, coughing was stimulated during the early postoperative period and deep breathing exercises insisted on. We realize that this causes some pain and discomfort but feel that it is a vital part of postoperative care. If sedation is given 20 to 30 minutes prior to ambulation or "stimulated coughing," the patient will be much more comfortable and will be better able to cooperate than if the medication is withheld. It should be stressed, however, that a patient should not be given too much sedation during the early postoperative period, since that would depress respiratory activity.

Seven patients, 7.3 per cent, had thrombophlebitis, five of them with pulmonary infarcts. One patient had signs and symptoms of a pulmonary infarct but no signs or symptoms of thrombophlebitis. All but one with symptoms of thrombophlebitis underwent bilateral ligation of the superficial femoral vein. We believe that all patients with signs and symptoms of thrombophlebitis should undergo bilateral ligation of the superficial femoral vein in conjunction with adequate anticoagulant therapy. Patients with signs of pulmonary infarction but without evidence of thrombophlebitis are given anticoagulant therapy alone.

Four patients, 4.2 per cent, had acute postoperative urinary retention. This complication will probably increase in frequency as time goes on because of the rise in the number of older patients subjected to operation. It should not be considered too lightly, therefore. We manage it in the following manner: If a patient is unable to void postoperatively, he is catheterized. If still unable to void, an indwelling Foley catheter is inserted and left in place for two days. At the end of this time the catheter is removed and the patient encouraged to void spontaneously. If after a reasonable length of time he is still unable to void, the indwelling catheter is reinserted for a two day period. If he is still unable to void at the end of this time, the catheter is left in place until such time as the obstruction can be removed surgically. Only one of our four patients required transurethral prostatectomy postoperatively.

FATAL COMPLICATIONS

There were six deaths following gastric resection in the 309 patients. Three of these were in patients under 50 years of age and three in patients over 50. Three deaths occurred in 1946, two in 1947, one in 1948 and none during 1949. Permission for autopsy was obtained in four cases, and the cause of death was definitely established in three. One patient in whom autopsy was limited to examination of the chest and abdomen was considered to have died from a cerebral accident, as this would have explained his clinical course and no other explanation was found. Two patients on whom autopsy was not performed died suddenly on their third postoperative day. One of these was believed to have died from coronary occlusion and the other from a pulmonary embolus.

The three remaining deaths were considered to result from technical failures. One of the patients involved was a 44 year old man with massive hemorrhage from a duodenal ulcer which was uncontrolled by medical regimen, including numerous transfusions. A large duodenal ulcer on the posterior wall rendered closure of the duodenal stump difficult. This opened, and generalized peritonitis resulted which was demonstrated at a secondary operation. The patient died on his sixth postoperative day. Another patient, a 47 year old man with massive hemorrhage, likewise failed to respond to conservative measures and was therefore subjected to an emergency operation. A large duodenal ulcer perforating into the pancreas and eroding the pancreaticoduodenal artery was found. In an attempt to remove the ulcer and control the bleeding, a suture was inadvertently placed about the intramural portion of the common duct. Five days after resection, the patient was again operated on and bile peritonitis was revealed, from which he died nine days after the first operation. At autopsy the defect in the common duct distal to its junction with the pancreatic duct was demonstrated together with the occluding suture. The duodenal stump was intact. The third patient had a marginal ulcer secondary to a gastroenterostomy done three years before. He was operated on for pain and vomiting. No difficulty was encountered in closing the duodenal stump after resection. The patient did well for two days after operation, and then symptoms of obstruction slowly developed but no pain or tenderness. Then followed a period of low grade sepsis, with death occurring 23 days after operation. Autopsy revealed a breakdown of the suture line of the duodenal stump, with abscess formation and multiple abscesses throughout the liver and kidneys.

Two of the three patients who died as a result of technical failure at operation demonstrated the hazard of resecting an ulcer of the duodenum in the presence of acute inflammatory reaction. This situation presents a difficult problem, for in years past we have lost patients from hemorrhage of a duodenal ulcer that had been left in situ after gastric resection. Eastman and Cole [5] and others have reported on series of patients who had no ensuing complications following gastric resection with the ulcer left undisturbed.

Although gastric resection is our procedure of choice for peptic ulcer and we have used it for 309 patients over the four year period presented, 1946 to 1949, other procedures have also been employed. During the same period, 35 patients were treated with gastroenterostomy and 82 with vagotomy, either alone or in combination with another procedure. Gastroenterostomy was employed only when there was specific contraindication to gastric resection. Usually the reason was debility in patients of advanced age or in patients with additional systemic disorders that rendered them poor operative risks for even the simplest procedure. In some instances the decision in favor of a gastroenterostomy was made at the time of operation, when inflammatory reaction associated with a perforating ulcer on the posterior wall of the duodenum made the surgeon feel that closure of the duodenum would be hazardous. Such compromise procedures have undoubtedly contributed to a lower incidence of complications and fatalities.

As stated above, 82 patients during the same period were treated with vagotomy, either alone or in combination with another procedure. However, like others, we have used this procedure cautiously. We first employed it for patients with marginal or jejunal ulcer following resection or gastroenterostomy. Our immediate results were spectacular and led us to use it as a primary procedure in a small series of 25 patients who would ordinarily have been treated with gastric resection. The immediate results with this group were not as successful but were still good. However, as time elapsed, the results became less satisfactory. Observations made from six months to two years after vagotomy have proved that 21, or 25.6 per cent, of the 82 patients must be rated as having obtained poor or unsatisfactory results. This trend has been in evidence for some time and has led us to limit the use of vagotomy to patients who for the most part have had marginal or jejunal ulceration following adequate gastric resection. It has also been used on patients who have had lesions secondary to gastroenterostomy when their condition was considered unsuitable for a more extensive procedure.

At the present time, we feel that an adequate gastric resection for duodenal ulcer should remove 65 to 75 per cent of the stomach as well as the portion of the duodenum containing the ulcer. If, however, it is felt that resection of the ulcerated duodenum will not permit satisfactory closure of the stump or that distortion of the adjacent structures might result in common duct injury even after insertion of a tube, then a compromise procedure should be done to exclude the ulcer temporarily. The aim in such a case would be to remove the ulcer at a later time. The only exception to this policy is an ulcer that is bleeding actively at the time of operation. We feel that the decrease in our mortality rate over the past four years has well justified this policy for the surgical treatment of peptic ulcer.

5. Eastman, W. H., and Cole, W. H.: Precautions and Results in Gastrectomy, Arch. Surg. **59**:768 (Sept.) 1949.

SUMMARY

A series of 309 patients with peptic ulcer treated with gastric resection is reviewed. The criteria followed in selecting these patients for operation is discussed. Preoperative preparation, extent and type of procedure and postoperative complications encountered are described. Brief reference is made to the other procedures, gastroenterostomy and vagotomy, employed during the same four year period.

CONCLUSIONS

Gastric resection for peptic ulcer can be accomplished with a low mortality rate.

The incidence of postoperative complications following gastric resection is still high, but it may be expected to decrease in the future.

Gastroenterostomy and vagotomy have a place in the surgical treatment of peptic ulcer, but they should be reserved primarily for cases in which gastric resection is contraindicated or has failed.

VAGOTOMY IN THE TREATMENT OF DUODENAL ULCER

Results in Three Hundred and Fifty Consecutive Cases

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THIS report summarizes our experience with 350 cases of duodenal ulcer subjected to bilateral vagotomy and followed for periods varying from six to 45 months. The project has been a joint responsibility of the Surgical Service and the Gastro-Enterology Section of the Medical Service, aided by the close collaboration of the departments of radiology, pathology and psychiatry.

TABLE 1.—*Primary Indications for Operation in the 350 Cases**

Intractable pain (54 of these also had a history of one perforation)	201	57%
Hemorrhage	118	34%
Pyloric obstruction	25	7%
Multiple perforations	6	2%

* In many patients there was more than one indication; however, the one that played the most important role in the decision to operate is given in this table.

SELECTION OF PATIENTS

In general, the indications for vagotomy in our patients have been similar to those usually considered for other types of surgery in the treatment of duodenal ulcer and its complications. Medical intractability was determined not only by a past history of inadequate medical response but also by the observation of the response to therapy under a rigid hospital program, usually for four weeks. It has been our experience that the chances of success with medical treatment are decidedly poor if the patient fails to show improvement with hospital therapy within this period. The primary indications for operation are summarized in table 1.

From Long Beach Veterans Administration Hospital.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

The ages of the patients ranged from 20 to 76 years (table 2) and the duration of illness from one month to 32 years, with 85 per cent of the patients having an established chronicity of the ulcer beyond a three year period.

DESCRIPTION OF SURGICAL PROCEDURES

The technic of vagotomy used at this hospital is essentially the same as that described by Dragstedt,[1] with several modifications.[2]

The operations in the series include vagotomy alone, either by the thoracic or by the abdominal approach, 83 cases; vagotomy with gastroenterostomy, 221 cases, and vagotomy with pyloroplasty of the Heineke-Mikulicz type,[3] 46 cases.

Vagotomy alone was performed in our earliest cases and therefore constitutes the group with the longest follow-up. Although the unmodified procedure gave excellent results as far as healing of the ulcer was concerned, the frequent occurrence of prolonged postoperative gastric retention made it advisable to add gastroenterostomy or pyloroplasty at the time of vagotomy. The thoracic approach was abandoned early in our experience because it did not permit the addition of a gastric

TABLE 2.—*Age Distribution*

Years	Cases
20 to 30	68
31 to 40	89
41 to 50	88
51 to 60	87
61 to 76	18

drainage procedure or the inspection of the pylorus and duodenum. Furthermore, it was found that the vagotomy could be accomplished as easily through the abdomen as through the thorax.[4]

While gastroenterostomy is a satisfactory means of providing gastric drainage, we have discontinued its routine use because of several occurrences of gastritis, one instance of intussusception of the jejunum through the stoma and one instance of marginal ulcer following incomplete vagotomy. Instead, we now use pyloroplasty,[5] which permits direct inspection of the duodenal ulcer, requires less time and is less likely to disturb the mucosa of the stomach by the regurgitation of the jejunal content.

1. Dragstedt, L. R., and Owens, L. M.: Supradiaphragmatic Section of the Vagus Nerves in the Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53**:152 (June) 1943.

2. Weinberg, J. A.; Campbell, G. W., and Voelker, R. B.: Vagus Nerve Section in the Treatment of Peptic Ulcer, J. Thoracic Surg. **17**:743 (Dec.) 1948.

3. Mikulicz, J.: Zur operativen Behandlung des stenosierenden Magengeschwüres, Arch. f. klin. Chir. **37**:79, 1888; cited by Finney, J. M. T., and Hanrahan, E. M., Jr., in Lewis, D.: Practice of Surgery: Clinical, Diagnostic, Operative, Postoperative, Hagerstown, Md., W. F. Prior Company, Inc., 1929, vol. 6, chap. 6, p. 60.

4. Weinberg, J. A., and Kraus, A. R.: Early Results from Vagus Nerve Section in the Treatment of Duodenal Ulcer: Report of 150 Cases, West. J. Surg. **56**:577 (Nov.) 1948.

5. Crile, G., Jr.: The Surgical Treatment of Peptic Ulcer, S. Clin. North America **28**:1123 (Oct.) 1948.

There have been eight reperformances of vagotomy because of evidence of inadequate denervation following the first operation. An intact right vagus nerve was found in seven of the patients and an intact left vagus nerve in one. All these patients have been completely relieved of ulcer symptoms after the second operation.

RESULTS

The cases included in this report have been evaluated on the basis of personal interviews and examinations at various intervals following operation and on the basis of answers to questionnaires. Follow-up studies for six months or longer have been obtained in 93 per cent of the 350 patients who underwent vagotomy between July 1946 and October 1949, inclusive. Four per cent have been followed by questionnaire alone and 89 per cent by return to the clinic for interview and examination as well as by questionnaire.

It is difficult to tabulate the results of vagotomy in patients with duodenal ulcer. Occasionally after vagotomy, even though the ulcer disappears as judged by all the criteria at our disposal, the patient continues to have symptoms. On the other hand, there are instances in which the signs and symptoms of ulcer disappear completely after operation but a crater can be demonstrated roentgenologically. How

TABLE 3.—*Results of Roentgenologic Examination*

Follow-Up Barium Studies	
Duodenum visualized	235
Presence of ulcer crater with recurrence of symptoms	6
Presence of crater with no symptoms	5
Duodenum not filled sufficiently to determine presence or absence of crater	102

are these patients to be classified? In the latter case, as far as the patient is concerned, he is cured. In the former, although one can find no evidence of ulcer, the patient continues to have symptoms. It is obvious that no one classification will cover the complex and varied postoperative results. We have therefore recorded the outcome on the basis of several criteria, namely, (1) results by roentgenologic examination, (2) results in relation to the primary indications, (3) results in patients with persistent symptoms who have undergone what we consider an adequate vagotomy, (4) postoperative responses to insulin, (5) results based on the postoperative symptoms as expressed by the patients, (6) undesirable side effects and (7) deaths.

1. RESULTS AS JUDGED BY ROENTGENOLOGIC EXAMINATION

Three hundred and forty-eight of the patients undergoing vagotomy had postoperative roentgenologic study of the gastrointestinal tract. The roentgenologists attempted to determine not only the status of the ulcer itself but also the completeness of the vagotomy. The latter was judged by the gastric peristalsis, motility, tone and size compared with those observed in the preoperative studies. They concluded from the postoperative studies that the vagotomy was adequate in 314 of the patients and inadequate in 34. Table 3 represents the most recent roentgenologic findings in the group of patients who had follow-up studies of six months or longer.

The five patients who were asymptomatic but showed roentgenologic evidence of a crater underwent an adequate vagotomy on the basis of laboratory studies

following operation. Of the six patients in whom an ulcer crater was visualized and who had a recurrence of symptoms, three had undergone an adequate vagotomy as determined by laboratory studies postoperatively and three had undergone what was considered an inadequate one.

2. Results According to the Effect of the Vagotomy on the Primary Indication for Surgical Treatment

Among the 201 patients in whom vagotomy was performed primarily for intractable pain there was a recurrence or persistence of symptoms in six instances (table 4). The following are abstracts of these cases.

Case 1.—The patient was a man aged 29. Pain recurred six months after vagotomy, and an ulcer crater was demonstrated by roentgenologic examination. The postoperative response of acid to insulin was positive. The symptoms have been controlled by medical management since the recurrence. We believe that this patient had an incomplete vagotomy.

Case 2.—The patient, a man aged 49, had a recurrence of ulcer pain 22 months after operation. The results of the studies made one month after operation were compatible with an adequate denervation. However, shortly after the recurrence of his symptoms, roentgen studies revealed the presence of an ulcer crater. The patient is to return for further observation.

Case 3.—A man aged 57 had a marginal ulcer after a gastroenterostomy for duodenal ulcer several years before his admission to our hospital. His symptoms recurred six months after vagotomy, and a marginal crater was again demonstrated on roentgenologic examination. Laboratory studies made postoperatively indicated that the vagotomy was incomplete. He is reluctant to accept further surgical treatment, since he is relieved by medical management.

Case 4.—A patient aged 43 had a recurrence of symptoms two years after vagotomy, with demonstration of a duodenal crater and a marked increase of free hydrochloric acid in response to insulin stimulation. His earlier postoperative studies had shown what appeared to be an adequate vagotomy. The patient has been managed well on a medical regimen, and further surgical intervention is not contemplated at this time.

Case 5.—The patient was a man aged 44 who had undergone vagotomy and gastroenterostomy for duodenal ulcer. The early postoperative studies indicated that the vagotomy was incomplete. His symptoms recurred after nine months, and a series of gastrointestinal roentgenograms revealed a duodenal and a marginal ulcer. A transthoracic vagotomy was then done at another hospital, and after this operation the laboratory studies still showed an incomplete vagotomy. One month later a subtotal gastric resection was done. Gastric analysis with insulin three months after the third operation again showed a notable rise of free hydrochloric acid in response to insulin stimulation. He was reoperated on, and an active marginal ulcer was found and resected. Gastrectomy at a higher level was also performed. No search was made for undivided vagal fibers.

Case 6.—The patient, a man aged 52, had undergone a vagotomy for a marginal ulcer, and results of laboratory tests made postoperatively were compatible with a complete denervation. He was asymptomatic for 18 months and then had a recurrence of his symptoms together with the demonstration of a marginal ulcer on roentgenologic examination. He is now being observed in the hospital.

Postoperative bleeding occurred in four of 118 patients in whom gastrointestinal bleeding was the prime indication for surgical intervention. Two of these reported the occurrence of tarry stools which they did not consider severe enough to warrant medical care. One patient bled on the third postoperative day and another during the third postoperative month. Additional surgical treatment has not been necessary for any of them.

Pyloric obstruction was the reason for operation in 25 patients, and in all these either a gastroenterostomy or pyloroplasty was performed with the vagotomy.

There were six patients in whom multiple perforations were the primary indication for surgical intervention. None of these has had a recurrence of perforation following vagotomy. There were 54 patients in the group with intractable pain who had had a single perforation. In none of these has reperforation occurred. In fact, there have been no known perforations in any of our cases after vagotomy.

3. Patients with Persistent Ulcer Symptoms Who Have Undergone What We Consider an Adequate Vagotomy

There have been five patients (1.5 per cent) in the followed group who have had persistence or recurrence of symptoms after what we considered to be an adequate vagotomy. Three of these patients have been discussed above in the abstracted

Table 4.—*Results in Relation to Primary Indications*

Indications	No. of Cases	Persistence or Recurrence
Intractable pain	201 (54 of these had single perforation)	0
Hemorrhage	118	4 { 1—hematemesis 3d postoperative day; 1—hematemeses 3d month; 2—history of tarry stools
Pyloric obstruction	25	None
Multiple perforations	6	None

Table 5.—*Postoperative Insulin Responses*

	No. of Cases
Insulin response in patients with no recurrence of ulcer:	
No rise	252
Rise { 1 to 10° — 45; 11 to 20° — 26; 21 to 30° — 8; 31 to 40° — 6; 41 to 87° — 5 }	90
Insulin response in patients with recurrence of ulcer:	
Rise, 28 to 60°	5
Patient being studied	1
Insulin test not done	2

reports of cases. The other two have had a recurrence of ulcer-like pain but have shown no demonstrable evidence of ulcer or gastritis at reexploration. Postoperative laboratory studies showed evidence of an adequate vagotomy in both of these patients. They were reoperated on because it was thought that other intra-abdominal lesions might be present which were not recognizable clinically. No cause for the pain could be found at exploration. The stomach and duodenum were opened, and the mucosa appeared normal.

4. Postoperative Responses to Insulin

Two hundred and fifty-two patients had no rise of free acid in response to insulin. Ninety of the patients followed up in whom there has been no evidence of recurrence or persistence of ulcer have shown an increase in free acidity in response to insulin. Of this group, approximately 50 per cent have shown a 1 to 10 degree rise after insulin stimulation; 29 per cent a rise from 11 to 20 degrees; 9 per cent from 21 to 30 degrees; 7 per cent from 31 to 40 degrees and 5 per cent

from 41 to 87 degrees. In the remaining eight cases there were five failures, classified as such because of persistence or recurrence of symptoms, and two deaths. In the five patients there was a high response of acid to insulin. There is one additional patient whose operation was classified as a failure who is being admitted for further insulin studies.

5. Opinions of the Patients Regarding the Value of the Operation

Of the 310 patients who replied to the questionnaire asking whether or not they were pleased with the operation, 288 stated that they were pleased with the results and 22 stated that they were not pleased. An additional group of answers obtained from verbal replies by 16 patients is included in the total evaluation given in table 6. With the exception of two patients, those with results described as poor (table 6) indicated that they were not pleased with the surgical result. The two patients in whom the results were classified as poor even though they were pleased with the

Table 6.—*Results Based on the Postoperative Symptoms as Expressed by the Patients*

Result	No. of Patients
Excellent (no complaints, no symptoms)	74
Good (mild temporary side effects; no symptoms of ulcer)	160
Fair (moderate temporary side effects; or mild symptoms controlled by diet or medication)	68
Poor (severe side effects or recurrence of ulcer symptoms)	24

Table 7.—*Analysis of Poor Results*

Follow-Up Period, Mo.	No. of Cases	Reason for Poor Result
31 to 45	6	2—recurrence of ulcer 2—gastritis 2—severe side effects
19 to 30	8	1—recurrence of ulcer 1—marginal ulcer 2—gastritis 4—severe side effects
6 to 18	10	2—recurrence of ulcer-like symptoms without demonstrable ulcer 3—gastritis 2—recurrence of ulcer 3—severe side effects

operation were included in this category because of protracted diarrhea in one case and repeated hypoglycemia-like attacks over a period of 18 months in the other.

An analysis of the poor results is shown in table 7.

6. Undesirable Side Effects

Retention.—In our early experience, a gastric drainage procedure was not performed concurrently with the vagotomy unless the patient demonstrated some degree of pyloric obstruction. Retention was one of the commonest undesirable side effects encountered. In 7 of the 83 cases in which vagotomy alone was performed a gastroenterostomy was added later because of persistent symptoms of retention. Since we have adopted the practice of routinely combining gastroenterostomy or pyloroplasty with vagotomy, this difficulty has been eliminated. In general, there has been a trend toward a return to normal gastric motility and tonicity within six to 12 months after vagotomy as demonstrated by roentgenologic studies.[6]

6. Isaac, F.; Ottoman, R. E., and Weinberg, J. A.: Roentgen Studies of the Upper Gastro-Intestinal Tract in Vagotomy, Am. J. Roentgenol. **63**:66 (Jan.) 1950.

Diarrhea.—Diarrhea occurred after vagotomy to some degree in 120 cases. In 90 of these it was mild and transient in nature, lasting from one to 10 days and with two to eight loose stools daily. In 25 it was more persistent, with attacks of one to three days' duration recurring at intervals of 10 to 14 days over periods of several months. In five cases the diarrhea has been classified as severe. In these cases it persisted for 12 to 15 months, with diarrheic episodes of two to three days' duration at intervals of five to 10 days. The patients with severe diarrhea are classified as having had poor results.

The onset of diarrhea occurred on the fifth to the fifty-third postoperative day, with the majority of patients having the onset within the first two weeks after operation.

Cardiospasm.—Cardiospasm has occurred in 24 of the cases and has been demonstrated roentgenologically in one third of those having this symptom. Roentgen examination was not made in the others as the condition was mild and transient in nature. The chief complaint was "difficulty in swallowing," with the patient usually commenting that the "food lodged in the chest." The onset took place during

TABLE 8.—*Summary of Undesirable Side Effects* *

Diarrhea		120
Mild	90	
Moderate	25	
Severe	5	
Cardiospasm		24
Hypoglycemic syndrome		81
Mild	53	
Moderate to severe	28	
Eructation and flatulence		28

* Two or more of the above side effects were present in the same patient in some instances.

a period ranging from the third postoperative day to the fifth month, occurring within the first three weeks after operation in all but four cases. The duration varied from two days to seven months, being from two to seven days in the majority. In cases in which the duration was longer the attacks occurred only occasionally. Relief was obtained in most cases by drinking a glass of hot water before meals. In the severer cases, intubation for 12 to 24 hours followed by a liquid diet for one or two days was sufficient to overcome the complaint. In no case was this side effect disabling.

"Hypoglycemic Syndrome."—A syndrome characterized by sudden weakness, sweating, tremor, nervousness and dizziness occurred in 81 cases. We refer to this as the "hypoglycemic syndrome" although actual hypoglycemia has been demonstrated in only a few of the patients complaining of this group of symptoms. The attacks usually come on from one to two hours after meals. The symptoms last only a few minutes and subside spontaneously. The time of onset of the attacks varied from the first to the fourth postoperative month. In 53 of the 81 patients the attacks were of a mild character and occurred only one to eight times. In the remainder of the cases they were more disturbing, and in four instances they were noted as often as four or five times weekly over periods of 12 to 18 months. The attacks were as prone to occur in those in whom a gastric drainage procedure was not performed as in those in whom it was, which fact suggests that the vagotomy itself plays an

important role in the cause of the syndrome. In most cases there has been a favorable response to a diet which is high in proteins, moderate in fats, low in carbohydrates and low in free sugar.

Eructation and Flatulence.—There was a group of patients, 28 in the entire series, in whom the predominant complaint following vagotomy was that of eructation and flatulence. None of these showed appreciable evidence of gastric retention or stasis on roentgenologic examination with a barium meal. The symptoms were not distressing.

7. Deaths

There have been two deaths in the series, one directly and the other indirectly attributable to vagotomy. The one directly due to the operation of vagotomy was in the eighth patient of the series. Death occurred on the seventh postoperative day as the result of pneumonitis. The diagnosis was made clinically and was confirmed by the autopsy findings. The second death occurred in a 48 year old patient with a 20 year history of duodenal ulcer. He entered our hospital after having had four surgical procedures in the two years prior to his entry, i. e., a gastroenterostomy, closure of a perforated marginal ulcer, a gastric resection combined with vagotomy and a transthoracic vagotomy. He continued to bleed from the gastrointestinal tract and to suffer from severe epigastric pain. On his admission the chest was reopened; two large vagal trunks were found, and segments were removed. The gastric acid level remained high, and his epigastric pain continued. A laparotomy was then performed, and the following pathologic changes were found: (1) a large marginal ulcer at the site of an anterior gastrojejunostomy of the Roux Y type and (2) a fistula between another loop of jejunum and the gastrojejunostomy site. The jejunojejunal fistula was repaired, the gastroenterostomy opening was closed and a gastrectomy was performed at a higher level. Death due to peritonitis occurred 17 days later.

COMMENT

A careful study based on answers to questionnaires and on return of the patients for roentgenologic examination, laboratory studies and personal interview indicates that vagotomy with pyloroplasty or gastrojejunostomy is a highly satisfactory means of dealing with the surgical problems of duodenal ulcer. The mortality is lower than any that we know of with other surgical procedures for duodenal ulcer. In the total number of cases, over 400 at the time this report was submitted for publication, there has been only one death directly attributable to the operation; one other death has been included only because the vagotomy failed to heal the ulcer which later resulted in the patient's death. There has been no morbidity due to perforation. Four patients in whom bleeding was suspected or proved had only one such occurrence, and none required treatment. In the analysis of the less tangible aspects of the ulcer syndrome, including symptoms of epigastric pain and indigestion, the results were also gratifying, with less than 7 per cent of the patients showing no benefit from the operation. The results in those benefited range from complete relief with no disturbing side effects of the operation to varying degrees of temporary side effects or occurrences of indigestion or pain without evidence of ulceration, which are well managed with dietary and other simple forms of medical treatment.

A significant number of our patients, 28 per cent, have shown healing and nonrecurrence even though the insulin tests showed a rise of free acid over the prestimulation levels. The several possible explanations for this are (1) that the healing is only temporary, (2) that complete vagotomy is not always necessary to effect healing or (3) that the insulin test is not infallible. Time and further study should give the answer.

A majority of the patients in this series have undergone either a gastroenterostomy or a pyloroplasty performed at the time of vagotomy in order to avoid the complication of considerable gastric retention which so often follows vagotomy alone. This raises the question, "Is it the vagotomy or is it the gastric drainage procedure which heals the ulcer?" In the cases in which vagotomy alone was performed, and in which the longest follow-up in our series (30 to 45 months) was carried out, there has been the same satisfactory healing of the ulcer as in cases in which gastroenterostomy or pyloroplasty was performed concurrently with vagotomy. This leads to the conclusion that the added drainage procedure is not necessary for the healing of the ulcer.

The most objectionable feature of vagotomy is the occurrence of undesirable side effects in a substantial number of patients. Gastric retention has been virtually eliminated as a disturbing factor by the performance of gastroenterostomy or pyloroplasty at the time of vagotomy. The other side effects usually present their greatest intensity in the first few weeks after operation and in most instances tend to subside gradually. Those that have required medical management responded well to such treatment in almost all instances. A valuable lesson which we have gained from our experience in dealing with these complications is that patients who have undergone the operation should be followed closely and managed carefully until readjustment of the gastrointestinal function has been accomplished.

Seven patients who underwent vagotomy and gastroenterostomy have been classified as having poor results because of the postoperative demonstration of gastritis on gastroscopic study. In these patients there is complete healing of the ulcer as judged by roentgen and laboratory studies but they still complain of epigastric pain. Inasmuch as they did not have a gastroscopic examination preoperatively, we are unable to say whether or not the gastritis antedated the vagotomy and the gastroenterostomy. It is felt that the use of pyloroplasty instead of gastroenterostomy will materially reduce the incidence of this complication.

Two patients have had a recurrence of abdominal pain similar to that experienced before vagotomy, despite the fact that there was no demonstrable evidence of ulcer or gastritis at reexploration. The recurrence or persistence of pain in the absence of evidence of an ulcer has been reported by others.[7] This impresses us as an important observation, for it suggests that vagotomy, like any other surgical procedure, may heal the ulcer and prevent its organic complications but may not necessarily relieve the patient completely.

In a review of these results it must be kept in mind that none of the patients has been observed for more than three and one-half years and many have been observed for only two years or less. A much longer period of observation is necessary before the value of vagotomy in the treatment of duodenal ulcer can be ascertained.

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7. Szasz, T. S.: Psychiatric Aspects of Vagotomy, Arch. Neurol. & Psychiat. **62**:728 (Dec.) 1949. Grimson, K. S.; Rundles, R. W.; Baylor, G. J.; Taylor, H. M., and Linberg, E. J.: Vagotomy: Observations During 4 Years, Surgery **27**:49 (Jan.) 1950.

SUMMARY

In the period from July 1946 to October 1949, 350 patients were subjected to vagotomy for duodenal ulcer and its complications. Of this number, 83 underwent vagotomy alone, 221 vagotomy with posterior gastroenterostomy and 46 vagotomy with pyloroplasty. Pyloroplasty is the drainage procedure being used at present. Of the 350 patients, 93 per cent have been followed for periods varying from six to 45 months.

In the 350 vagotomies performed there were two deaths, a mortality of 0.57 per cent.[8]

The results of operation are analyzed on the basis of roentgenologic examinations, the effect of vagotomy on the primary indications for surgical treatment, postoperative insulin responses, the opinions of the patients regarding the value of the operation, the postoperative symptoms and the undesirable side effects.

8. At the time this report was submitted, the number in the series had increased to 430, without any additional deaths.

COMBINED PROCEDURE OF PARTIAL GASTRECTOMY AND INFRADIAPHRAGMATIC VAGUS RESECTION

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AT THE TIME of the inception of this study an adequate partial gastrectomy was the standard procedure used in the treatment of patients with peptic ulcer requiring surgical treatment in this hospital. It was our opinion, in view of the frequent necessity to use supplemental vagotomy and the paucity of long term results for interpretation, that the latter procedure was to be considered at this time as an adjunct in peptic ulcer therapy, and it seemed most plausible to use it as such along with the procedure which in our hands and in the hands of others had heretofore given the best results. It was our purpose to determine whether the addition of vagus neurectomy could improve our results in the surgical treatment of duodenal ulcers sufficiently to make it a practical supplement in future therapy. Operations other than partial gastrectomy allow acid and pepsin secreting glands to remain in significantly large numbers. Despite their release from cephalic stimulation as a result of vagotomy, these glands retain autonomous secretory function. Through continued local stimulation and irritation, with resultant hyperchlorhydria, recurrent ulcers have developed in cases in which either a vagotomy or inadequate gastric resection has been performed.[1] Therefore, it was decided to use bilateral infradiaphragmatic vagus resection in conjunction with partial gastric resection in approximately 25 consecutive patients with duodenal ulcer requiring surgical treatment. It was realized that a percentage of these patients would have been treated by vagotomy alone in many clinics, but to make interpretation of our results valid case selection could not be permitted.

We derived encouragement from the report of the work done by the group at the Mount Sinai Hospital in New York city, who published a preliminary report in 1929. Klein[2] reported on eight patients treated by partial gastric resection and a left vagus section. These patients were selected because of the high acidity found preoperatively on gastric studies. All his patients had a complete absence

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Wilbur, D. L.; Cheney, G., and Mathewson, C.: Clinical Conference on Vagotomy, M. Clin. North America **32**:301, 1948.

2. Klein, E.: Left Vagus Section and Partial Gastrectomy for Duodenal Ulcer with Hyperacidity, Ann. Surg. **90**:65, 1929.

of free acid in the three hour Rehfuss test meal six months after operation. In a controlled group, without the vagotomy, only 25 per cent of the patients showed comparable results. Winkelstein and Berg [3] carried on the work of Klein at Mount Sinai Hospital, and in 1938 they published further data on the combined procedure. They performed this operation on 34 patients with duodenal ulcer with a free acidity of over 40 degrees. Fourteen per cent of these patients had a persistence of free acidity postoperatively the amount of which averaged 23 degrees. There were no recurrences, and no ill effects could be ascribed to the vagotomy. Klein's cases are assumed to be included in this series as the follow-up time ranged upward to 9.5 years.

Lahey [4] in the early part of 1947 stated that he was employing infradiaphragmatic vagotomy in most of the patients on whom partial gastrectomy was being performed in an effort to reduce recurrent jejunal ulcers and to prevent postoperative bleeding. In this same year Johns and Grose [5] reported on the use of vagotomy in conjunction with splanchnicotomy, enterostomy, pyloroplasty and partial gastric resection in peptic ulcer therapy.

The over-all results were felt to be 100 per cent satisfactory in cases in which resection was performed and in those with procedures in which a stoma was established, in comparison to an incidence of satisfactory results of 79 per cent in patients treated with vagotomy alone. Subsequent gastroscopic findings in these patients were reported by Paulson and Gladsen.[6] These observers felt that the stomal openings were larger than those generally seen in subtotal gastrectomy and that the mucosal changes were similar to the gastritis seen in cases of subtotal gastric resection without vagotomy. They concluded by stating that vagotomy gives no protection against postoperative gastritis and jejunitis.

Gardner [7] expressed the opinion that combined vagotomy and gastric resection is particularly indicated in cases of peptic ulcer when there is (1) a high acidity, (2) anxiety on the part of the patient, with a tendency to the development of stomal ulcers, and (3) difficulty in the mobilization of the first part of the duodenum. In 22 patients treated none of the complications of simple vagotomy was experienced at the time of their discharge from the hospital.

Colp [8] and his associates believe that the combined procedure is especially indicated for patients with duodenal ulcer in whom bleeding without pain is a predominant symptom as well as for those patients who have unusually high preoperative gastric acidity. They compare 46 patients treated in this manner with 54 patients treated by means of gastric resection alone during the same period.

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3. Winkelstein, A., and Berg, A. A.: Vagotomy Plus Partial Gastrectomy for Duodenal Ulcer, Am. J. Digest. Dis. & Nutrition **5**:497, 1938.

4. Lahey, F. H.: A Position on the Employment of Vagotomy in the Surgical Treatment of Peptic Ulcer, Lahey Clin. Bull. **5**:66, 1947.

5. Johns, T. N. P., and Grose, W. E.: Symposium on Vagotomy for Peptic Ulcer: Early Surgical Results in 43 Cases, Bull. Johns Hopkins Hosp. **81**:92, 1947.

6. Paulson, M., and Gladsen, E. S.: Medical Aspects of Vagotomy for Peptic Ulcer, Including Observations on Clinical Value of Insulin Test and on Post-Operative Criteria for Completeness of Bilateral Gastric Vagus Section, Bull. Johns Hopkins Hosp. **81**:107, 1947.

7. Gardner, C.: Simultaneous Vagotomy and Partial Gastrectomy for Intractable Peptic Ulcer, Canad. M. A. J. **58**:137, 1948.

8. Colp, R.; Klingenstein, P.; Druckerman, L. J., and Weinstein, V. A.: A Comparative Study of Subtotal Gastrectomy With and Without Vagotomy, Ann. Surg. **128**:470, 1948.

There were no deaths in this group of 100 patients. The early postoperative course was not as smooth in the patients treated by the combined procedure, and complications were approximately twice as common as in those treated by partial gastrectomy. This was largely the result of pulmonary complications, abdominal distention, dysphagia, duodenal fistulas and intraperitoneal exudates occurring in the former group. Postoperative studies of the group treated by the combined procedure showed 100 per cent achlorhydria in the gruel test, 95 per cent achlorhydria in the night secretion and 75 per cent in the histamine test, with 83 per cent achlorhydria on insulin gastric analysis.

Of 40 patients treated with the combined procedure, 85 per cent were well and 15 per cent improved, and in no case did a jejunal or recurrent ulcer develop. As a group, these patients responded slightly better to treatment than did the group on whom partial gastrectomy was performed.

Sanders [9] recently stated that he is performing the combined gastric resection and vagus resection for patients with gastric ulcers who come for surgical treatment. His results have not been published.

It is intended that this presentation be considered as a preliminary report, since it is felt that the results of treatment of peptic ulcers must be based on an adequate and extended follow-up study covering many years.

RESULTS

The series of cases presented represents a group of 25 patients who, according to accepted surgical dictum, required operation for duodenal ulcer. These were patients admitted consecutively to the surgical service from July 1947 to August 1948. The first operation of this type was performed on July 9, 1947, and the last on Aug. 11, 1948. In each case the operative procedure accomplished was identical in every respect. A bilateral subdiaphragmatic vagus resection was accomplished together with a partial gastrectomy which was similar to other resections performed for peptic ulcer at this hospital during the past three years.

The average duration of symptoms was 11 years, the shortest being 1½ years and the longest 30 years. The average age of the patients was 44.6 years, the youngest being 21 and the oldest 59.

Thirty-two per cent of the patients had undergone a previous gastric operation; six patients, or 24 per cent, had been subjected to suture of a perforated ulcer and two, or 4 per cent, had undergone a previous gastroenterostomy (table 1). Forty per cent of these patients had repeated or massive gastrointestinal hemorrhages. Three had an associated gastric ulcer which was resected at the time of operation. Twenty per cent had pyloric obstruction prior to operation (table 1).

All the patients were followed for 11 to 24 months, and they were readmitted for hospital survey after six months. Six patients returned for study because of symptoms, and the remainder were followed up by means of a questionnaire in December 1948. Twenty-four per cent of all the patients had some type of postoperative complaint; of this group 16 per cent may be considered troublesome and undesirable. Three, or 12 per cent, complained of occasional diarrhea, lasting one

9. Sanders, R. L., in discussion on Aaron, A. H.; Lipp, W. F., and Milch, E.: Newer Aspects of Peptic Ulcer Therapy, J. A. M. A. **139**:519 (Feb. 19) 1949.

TABLE 1.—*Vagectomy and Partial Gastrectomy*

Patient	Age, Yr.	Duration of Symptoms	Complications	Previous Operations	Location and Type of Lesion	Date of Operation	Postoperative Complications	Postoperative Complaints and Duration of Follow-Up	Preoperative Gastric Analysis, HCL Value	Total	Free	Postoperative Gastric Analysis, Insulin Test	Results
H. J. H.	53	7	0	0	Chronic duodenal ulcer; pyloric obstruction	7/ 9/47	0	0 17 mo.	.....			No free HCL No increase	Good
F. F. E.	54	2	Bleeding ulcer, 3 times	0	Healed duodenal ulcer	7/14/47	0	Loss of weight and gastritis 22 mo.	.....			No free HCL No increase	Good
L. M.	57	4	1 hemorrhage	0	Chronic duodenal ulcer; gastric ulcer; cholelithiasis	7/21/47	0	0	Fasting 1st specimen	24° 40°	10° 30°	No free HCL No increase	Excellent
F. W. C.	59	25	0	0	Chronic duodenal ulcer; pyloric obstruction; diverticulum, stomach	7/25/47	Jaundice from transfusion reaction	Occasional weakness 17 mo.	Fasting 1st specimen	31° 30°	0° 0°	No free HCL No increase	Good
C. I. C.	32	11	Bleeding ulcer, 2 times	0	Healed duodenal ulcer; fibrosing duodenitis	7/31/47	0	Emotional instability, loss of weight, 1 mo.; diarrhea and vomiting, intermittent on occasions	Fasting 1st specimen	70° 52°	51° 40°	No free HCL No increase	Fair
V. P. S.	48	5	Perforated ulcer	Perforated ulcer, 1945	Chronic duodenal ulcer; pyloric obstruction	8/ 7/47	Mental confusion 1 wk.	Occasional vomiting, food dyserasia 16 mo.	Fasting 1st specimen	65° 88°	31° 70°	No free HCL No increase	Good
H. L.	54	10	2 hemorrhages	0	Chronic duodenal ulcer	8/13/47	0	Loss of weight; occasional diarrhea 19 mo.	.....			No free HCL No increase	Good
I. J. F.	51	15	Perforated duodenal ulcer, 1940	Perforated duodenal ulcer	Chronic duodenal ulcer	8/15/47	0	Now a diabetic 16 mo.	Fasting 1st specimen	72° 20°	40° 8°	No free HCL No increase	Good
V. C.	33	13	0	0	Anterior and posterior duodenal ulcers	8/28/47	Peritonitis, acute; duodenal perforation; pericardial effusion; traumatic pericarditis	0 16 mo.	Fasting 1st specimen	32° 32°	13° 18°	No free HCL No increase	Excellent
J. O.	43	3	2 massive hemorrhages	6	Chronic duodenal ulcer; healed gastric ulcer	9/ 2/47	Penicillin reaction, severe; dysphagia 1 mo., and jaundice 2 mo. after surgery	Dysphagia 1 mo. 15 mo., normal	.....			No free HCL No increase	Good
E. E. B.	46	4	Perforated ulcer, 1946	Perforated ulcer, 1946	Chronic duodenal ulcer	9/ 3/47	0	0 15 mo.	Fasting 1st specimen	73° 67°	46° 45°	No free HCL No increase	Good

R. H.	28	1½	Massive hemorrhage	0	Chronic duodenal ulcer	9/11/47	0	0 15 mo.	.....			No free HCL No increase	Good
G. S.	41	4	Alcoholism	0	Kissing ulcer; diverticulum, duodenum	9/15/47	Generalized peritonitis; duodenal perforation	Abdominal pain and distention	Fasting	59°	32°		Died 9th postoperative day
F. P.	55	25	0	0	Chronic duodenal ulcer; pancreatitis	9/16/47	0	0 15 mo.	.....			No free HCL No increase	Excellent
H. S.	42	21	2 hemorrhages	Gastroenterostomy, 1937	Chronic duodenal ulcer; marginal ulcer; pancreatitis	9/16/47	0	0 18 mo.	Fasting 1st specimen	65° 60°	43° 35°	No free HCL No increase	Excellent
E. S. M.	50	20	0	0	Chronic duodenal ulcer; pancreatitis	9/26/47	0	0 15 mo.	Fasting 1st specimen	90° 25°	0° 12°	No free HCL No increase	Excellent
W. D. B.	51	10	0	0	Posterior duodenal ulcer; pancreatitis; diverticulum, duodenum	9/29/47	0	0 15 mo.	Fasting	45°	26°	No free HCL No increase	Excellent
W. B.	53	18	Perforated ulcer	Perforated ulcer	Gastric and posterior duodenal ulcer	10/ 3/47	0	0 14 mo.	Fasting 1st specimen	25° 37°	4° 13°	No free HCL No increase	Excellent
C. L. H.	35	8	2 hemorrhages	0	Kissing duodenal ulcer	12/16/47	Bleeding from anastomosis for few days	0 12 mo.	Fasting 1st specimen	55° 70°	28° 56°	No free HCL No increase	Good
L. L. B.	26	7	Marginal ulcer	Gastroenterostomy, 1942	Marginal ulcer; chronic duodenal ulcer; obstruction, jejunal	1/ 5/48 1/21/48	Intestinal obstruction	0 16 mo.	Fasting 1st specimen	54° 70°	28° 56°	No free HCL No increase	Good
W. F. B.	21	4	Massive hemorrhage and shock	0	Posterior duodenal ulcer	1/14/48	0	0 12 mo.	.....			No free HCL No increase	Good
B. M. F.	52	30	Massive hemorrhage, 1939	Cholecystectomy, 1932	Healed duodenal ulcer	1/16/48	0	0 17 mo.	.....			No free HCL No increase	Excellent
S. A. D.	53	8	0	0	Gastroduodenitis; healed ulcer	2/15/48	Hematoma wound	0 22 mo.	.....			No free HCL No increase	Good
I. J. K.	40	15	Ruptured ulcer; pyloric obstruction	Ruptured ulcer, 1948	Chronic duodenal ulcer; pyloric obstruction	4/27/48	0	Diarrhea, 8 mo.	.....			No free HCL No increase	Good
F. J. W.	35	5	Hemorrhage; ruptured ulcer	Ruptured ulcer, 1946	Chronic duodenal ulcer; pyloric obstruction	8/11/48	0	0 9 mo.	.....			No free HCL No increase	Good

to three days and consisting of two to six loose bowel movements daily. One had symptoms which might be considered as a "dumping syndrome."

Six patients who returned because of symptoms were examined by means of gastroscopy in addition to the routine physical and laboratory examinations. All these showed evidence of acute gastritis. (In the future follow-up studies, all patients will be given gastroscopic examination and will be compared with a similar group who underwent partial gastrectomy without vagus resection.) However, the endoscopist was of the opinion that the gastritis seen in the six cases did not differ in type or severity from that in several cases observed after the routine type of partial gastrectomy.

Seventeen, or 68 per cent, of all the patients stated that they felt better after operation than before. Ten were free from pain, and 14 complained of occasional mild abdominal pain. The majority were on a liberal diet, and 10 of them stated that they were able to eat all foods without feeling any discomfort. The remainder had mild nausea or occasional vomiting if they overate or if they consumed highly seasoned or fried foods.

In every instance there was a complete severance of all fibers of the vagus nerves as evidenced by Hollander's insulin test, after which there was no evidence of free hydrochloric acid (table 1), increased total acidity or increased quantity of gastric secretions. In all cases in which follow-up studies were made six to 18 months after surgical intervention there was no change from this state of anacidity. The preoperative gastric secretion studies revealed in most instances the usual hyperchlorhydria found in patients with duodenal ulcer (table 1). There was no evidence of regeneration of the vagus nerves in any of the cases, the longest follow-up period being 18 months.

Although these repeated studies are based on a small number of cases, it is signifieant to note that the vagus resection combined with partial gastrectomy resulted in achlorhydria in all patients. It may be possible that further studies and investigations of the cases for a longer period may bring about a reasonable explanation of this consistent finding.

Roentgenologic studies were carried out in the majority of instances. These consisted of examination of the upper part of the gastrointestinal tract and motor meal studies of the small bowel. In every instance the remaining portion of the stomach revealed dilatation and atonicity, with some delay in the emptying time as compared with that in cases in which partial gastrectomy without vagus resection was performed. The newly created stoma in all cases revealed normal function.

It has been shown in many other series,[10] as well as in our own cases in which a Polya type of gastric resection with a wide stomal anastomosis was done, that the emptying time of the stomach after a barium meal was rapid, usually complete within 45 to 60 minutes. However, after this combined procedure the emptying

10. Gilbert, J. A. L., and Dunlap, D. M.: Hypoglycemia Following Partial Gastrectomy, Brit. M. J. **2**:330, 1947. Porter, H. W., and Claman, Z. B.: A Preliminary Report on the Advantages of a Small Stoma in Partial Gastrectomy for Ulcer, Ann. Surg. **129**:417, 1949. Shay, H., and Gershon-Cohen, J.: Experimental Studies in Gastric Physiology in Man: Mechanism of Gastric Evacuation After Partial Gastrectomy as Demonstrated Roentgenologically, Am. J. Digest. Dis. & Nutrition **2**:608, 1935. Strauss, A. A., and others: Physiological and Clinical Study of Patients After Subtotal Gastrectomy, Am. J. Digest. Dis. & Nutrition **4**:32, 1937. Vitkin, S. F.: Motor Functions of Stomach After Resection, Ann. Surg. **111**:27, 1940.

time was delayed, and after barium meal studies the stomach emptied in one and a half to three hours. The barium sulfate seemed to be suspended high in the dilated atonic remaining portion of the stomach (figs. 1 to 5).

Fig. 1.—Preoperative barium studies of stomach and small bowel prior to (*A*) partial gastrectomy and vagectomy and (*B*) partial gastrectomy.

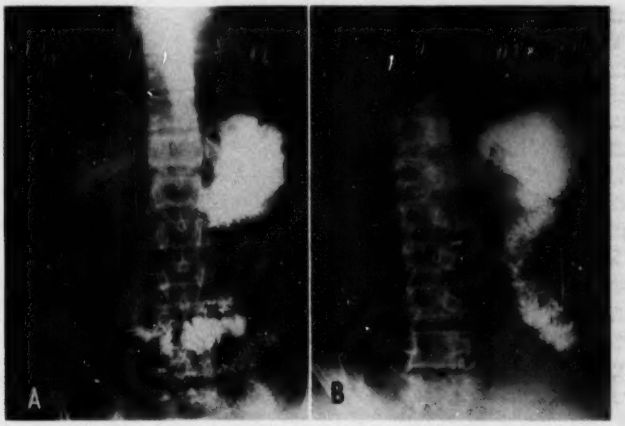

Fig. 2.—Postoperative barium studies of stomach and small bowel after combined procedure (*A*) and after partial gastrectomy (*B*). Roentgenograms were taken shortly after filling of stomach remnant with barium.

The motor meal studies revealed a normal pattern of the small bowel and normal transit time except in two instances. In both of these there was evidence of hypomotility of the small bowel and segmentation of the barium column. These conditions persisted for at least six months after surgical intervention.

In spite of complaints in a few cases, the results to date were considered good to excellent. The 16 per cent of patients having complaints indicated an increase of 6 to 8 per cent over patients with peptic ulcer who were treated with the same

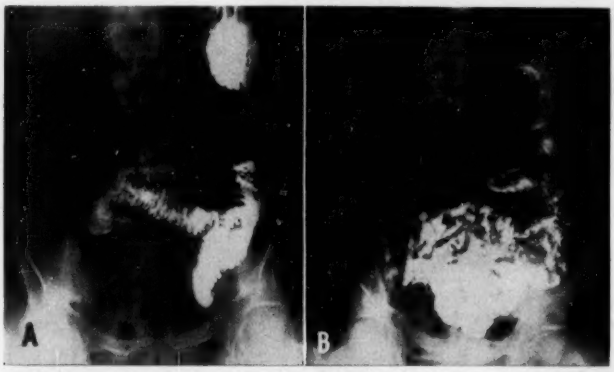

Fig. 3.—Roentgenograms made one hour after a barium sulfate meal in a case in which a combined procedure was carried out (*A*) and one in which partial gastrectomy was performed (*B*). Delayed emptying of barium from gastric remnant and associated gastroplegia are revealed in *A* as compared with *B*, in which a more rapid emptying has occurred and gastroplegia is absent.

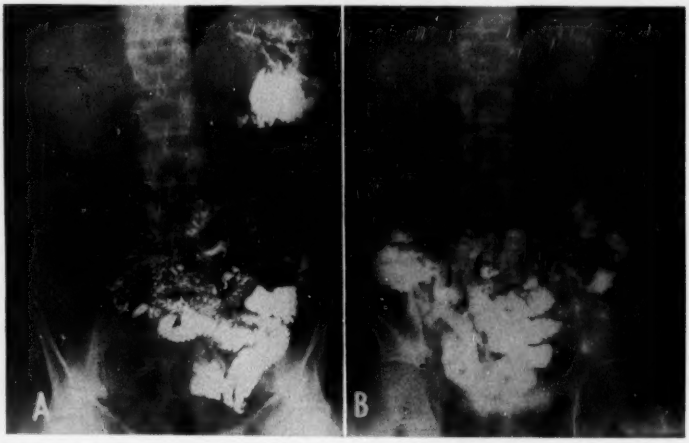

Fig. 4.—Roentgenograms made two hours after a barium sulfate meal in a case in which a combined procedure was carried out (*A*) and one in which partial gastrectomy was performed (*B*). Note the amount of barium in the small bowel and the stomach in *A*. In *B* the stomach is completely empty and there is evidence of barium in the ascending colon.

type of partial gastrectomy without vagus resection. (It is intended to present a paper showing, as a preliminary report, a comparison of the results in this group with those in a group in which partial gastrectomy alone was carried out.)

During the operation, or immediately after, there were no circulatory changes or effects which are ascribed to vagus resection such as bradycardia, vagovagal reflex or cardiac arrest. However, in one case a longitudinal tear of the muscular wall of the esophagus occurred while the esophagus was being mobilized and the vagus nerves freed. The vagus nerves were sectioned, and the patient experienced dysphagia for about one month. In repeated follow-up studies he experienced no difficulty in swallowing, although fluoroscopic examination of the esophagus with barium sulfate revealed some achalasia.

POSTOPERATIVE COMPLICATIONS

There was one death (a mortality rate of 4 per cent) in this series, occurring in a male, a chronic alcoholic, 41 years of age. He died on the ninth postoperative day from generalized peritonitis and subphrenic abscess due to leakage from the duodenal stump.

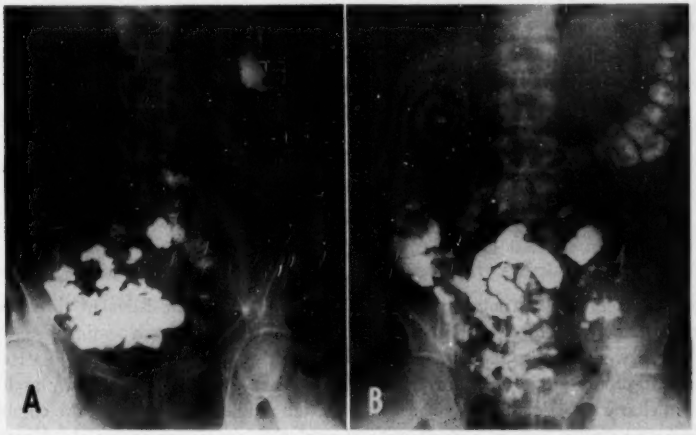

Fig. 5.—*A*, roentgenogram made six hours after a barium sulfate meal in a case in which a combined procedure was carried out. Note small amount of barium in the stomach and the remainder in the terminal loops of small bowel. *B*, roentgenogram made three hours after a barium meal in a case in which partial gastrectomy was performed. Complete emptying of stomach is seen, with barium in the colon and small bowel.

The complications (table 2) which developed were those commonly seen following gastric surgery except in two cases. In these instances the addition of vagus resection to the partial gastrectomy was responsible for two unusual complications. As mentioned above, dysphagia developed in one patient as a result of trauma to the muscular wall of the esophagus, and in the second case a hemorrhagic type of pericarditis developed, which we feel may have been the result of trauma to the pericardium during mobilization of the esophagus from below through the esophageal hiatus of the diaphragm. In this same patient peritonitis developed from a duodenal fistula which closed spontaneously.

There was one case of homologous serum jaundice that was not unusually severe. In another patient obstruction to the jejunal loop developed requiring an

enteroenterostomy. This patient had a marginal ulcer at the site of the previously performed gastroenterostomy and also an active duodenal ulcer, both of which were removed and an old gastroenterostomy undone.

In another case there was active bleeding for several days from the stomach. This was assumed to be coming from the site of the anastomosis.

COMMENT

There were two cases in which complications developed as a direct result of the addition of subdiaphragmatic vagus resection to partial gastrectomy. The operative death in this series was not directly attributed to the operation of vagectomy per se but was as a result of complications common to partial gastric resection.

The delayed emptying time of the gastric remnant resulting from gastric atony and dilatation as a result of vagus resection in this group of cases may be another desirable feature of a combined procedure in that it prevents a too rapid emptying of the stomach and thereby eliminates one of the possible causes of the dumping

TABLE 2.—*Postoperative Complications*

Diarrhea, mild, occasionally	3
"Dumping syndrome"	1
Duodenal fistula	2
Dysphagia	1
Gastritis	6
Hemorrhage from anastomosis site	1
Hemorrhagic, pericarditis, traumatic	1
Homologous serum jaundice	1
Intestinal obstruction	1

syndrome. This syndrome is theoretically explained on the basis of three possibilities, namely, distention of the jejunum, jejunitis or hypoglycemia.

There were no instances of severe or persistent diarrhea as seen in cases in which vagotomy alone is performed. The diarrhea occurred occasionally and was mild in character. Postoperative gastric secretion studies revealed that the combined procedure resulted in a persistent state of achlorhydria. This factor alone appears significant, and generally it is felt that with this type of anacidity development of marginal or jejunal ulcers is precluded. There is no evidence to date of any signs, symptoms or findings of recurrent ulcers in this series, but it is felt that a longer period of observation is necessary before definite conclusions can be made in this regard.

It is the opinion of one of us (L. T. P.) that by combining vagus resection with gastric resection, a less radical gastrectomy could be accomplished, and some of the undesirable features of that operation thereby eliminated. On the other hand, the type of anastomosis performed in gastric resection obviates some of the sequelae of vagotomy alone. The removal of the duodenal ulcer and the prepyloric area of the stomach and adequate vagus resection below the diaphragm should exclude the main factors responsible for the development and continued activity of peptic ulcer. This measure will eliminate the cephalic phase of gastric secretion, resulting in achlorhydria in most instances; the removal of the ulcer-bearing areas of the stomach and duodenum will reduce the incidence of ulcers; the creating of an

adequate ostium for proper emptying of the stomach will prevent undesirable features of vagotomy alone, and the retention of sufficient stomach will provide the patient with an adequate gastric remnant for an average intake of food at meal time without increasing to any degree the mortality or morbidity rates of a more radical gastrectomy.

It was felt that after a long period of satisfactory observation and follow-up of this group a second series of operations consisting of infradiaphragmatic vagus resection with a minimal gastric resection should be carried out as outlined above.

SUMMARY

The operative mortality following the combined procedure of infradiaphragmatic vagus resection and partial gastrectomy was not increased per se by the addition of the vagus resection. The immediate postoperative morbidity rate was increased by the addition of this procedure to partial gastrectomy. There was achlorhydria in all cases after the combined procedure. The majority of disabling symptoms seen after vagus resection alone were not present in this series of cases. The combined procedure, because of the achlorhydria and absence of gastrospasm, should diminish the incidence of marginal or jejunal ulcers. The delayed emptying time may be a desirable feature of this operation in eliminating one of the possible causes of the dumping syndrome. A longer period of follow-up studies in this group will indicate whether infradiaphragmatic vagus resection combined with partial gastrectomy lowers the incidence of recurrent ulcers and whether a less radical gastric resection may be safely attempted.

ADDENDA

Since the preparation of this article, five additional operations were performed. To date the results from this group are similar to those in the 25 cases reported above.

At the present time the entire series of 25 patients are being recalled for a complete study. Of this total number, seven were examined in December 1950. The twelve hour fasting gastric secretions averaged 350 cc.; 40 per cent of the group had gained 14 pounds (6.4 Kg.) in weight and the remaining 60 per cent were maintaining their preoperative weight. Forty per cent had occasional attacks of diarrhea, and the same per cent had no diarrhea. One patient had diarrhea frequently. There was a persistent and constant absence of free hydrochloric acid in the fasting specimen and after the histamine and insulin tests in all the cases studied. The majority of patients revealed gastritis on gastroscopic examination; however, most of them had no complaints referable to the stomach. The majority of the patients were on a liberal diet. A few experienced some distress on overloading their stomachs, and in some instances certain foods caused symptoms.

The roentgenologic studies revealed retention of barium and delayed emptying time of the stomach from two to six hours in 71 per cent of this group of cases. In two, or 29 per cent, of the recent group studied there was a disturbance in the small bowel motor pattern characterized by segmentation of the barium column. The small bowel transit time, however, was normal in the entire series.

During the later half of 1949, seven other patients of this series were recalled for study. The findings in this group corresponded with those in the seven patients recently examined.

It is interesting to note that in the entire series there was a complete absence of free hydrochloric acid in all the tests performed, including fasting, histamine and Hollander's insulin tests, after surgical treatment and that this absence has persisted in the entire group during frequent follow-up studies, which now have covered a period of 28 to 41 months.

The Department of Radiology reviewed and interpreted the gastrointestinal studies in this series.

PHYSIOLOGICAL AND CLINICAL STUDIES OF VAGOTOMIZED PATIENTS

A Study of Three Hundred and Thirty-One Patients

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THE REINTRODUCTION of gastric vagotomy in the treatment of duodenal, gastric and gastrojejunal ulceration by Dragstedt[1] in 1946 has stimulated a wide interest in this operation. Previous reports by one of us[2] have always advocated a reservation of opinion regarding postoperative clinical results because of the relatively short follow-up period. However, we now consider that follow-up studies from one to four years after operation have been carried out on a sufficient number of the 331 patients who have undergone gastric vagotomy at the Mayo Clinic so that some opinions can be formulated as to the comparative clinical value of gastric vagotomy in the treatment of the various types of peptic ulceration. In addition, the long term effects of gastric vagotomy on gastric acidity and motility and the results of insulin tests and their value as prognostic indexes of clinical results can be evaluated.

Our study is based on three series of cases (table 1). Series 1 consists of 141 cases in which operations were performed on one of the surgical services at the Mayo Clinic during the past five years. Clinical and laboratory follow-up studies were performed in 87; replies by questionnaires were obtained in an additional 25. Twenty-three patients operated on during the past year are not included in the postoperative study of conditions one to four years after operation, and two patients have not been traced (one lives in Iceland and another is an itinerant cowboy). There were three hospital deaths, and one patient died at home eleven months after operation. There were 10 proved (table 2) and four suspected (table 3) recurrences of ulcer in series 1. Series 2 consists of 190 cases in which operation was performed on the remaining combined surgical services at the Mayo Clinic

From the Division of Surgery, Mayo Clinic (Dr. Walters) and Mayo Foundation (Drs. Belding and Lillie, Fellows in Surgery).

1. Dragstedt, L. R.: Section of the Vagus Nerves to the Stomach in the Treatment of Gastro-Duodenal Ulcer, Minnesota Med. **29**:597-604 (June) 1946.

2. (*a*) Walters, W., and Fahey, M. M.: Influence of Vagotomy on Peptic Ulcer, Gastric Acidity and Motility: A Follow-Up Study on 68 Patients and Evaluation of the Operation, Arch. Surg. **61**:86-94 (July) 1950. (*b*) Walters, W.; Brownson, B. C., and Phillips, S. K.: The Problem of Vagotomy in the Treatment of Peptic Ulcer, Kentucky M. J. **47**:254-262 (July) 1949. (*c*) Walters, W.: Vagotomy in the Treatment of Peptic Ulcer, Practitioner **162**:33-35 (Jan.) 1949; (*d*) The Results of Vagotomy: Follow-Up of 29 Patients, Practitioner **162**:232-234 (March) 1949.

during a similar period; cases in which operations were performed less than a year ago are not included in these. Of this group, 43 patients returned for laboratory

TABLE 1.—*Vagotomy in Series 1, 2 and 3*

Operation	Series *	Cases	Duodenal	Gastrojejunal	Gastric	Gastric and Duodenal
Vagotomy only	1	60	24	26	10	..
	2	57	15	42	..	..
	3	991	741	250	..	..
Vagotomy and gastroenterostomy	1	54	52	..	2	..
	2	109	105	..	2	2
	3	1,046	1,046	..	..	..
Vagotomy and pyloroplasty	1	8	6	..	2	..
	2	6	5	..	1	..
	3	114	114	..	..	..
Vagotomy and gastric resection	1	14	9	5	0	..
	2	12	4	6	2	..
	3	407	353	..	54	..
Vagotomy and take down	1	5	..	5	..	..
	2	6	..	6	..	..
	3	..	..	..	..	..
Total	1	141	91	36	14	..
	2	190	129	54	5	2
	3	2,558	2,245	250	54	..
Grand total	..	2,889	2,465	340	73	2

* Series 1, Mayo Clinic—Total cases of one of the authors (Walters). Series 2, Mayo Clinic—Total cases of other surgeons. Series 3—Collected series of Vagotomy Committee of the American Gastroenterological Association, 1950.

TABLE 2.—*Proved Recurrence of Ulcer in Series 1 and 2*

Ulcer and Associated Operation	Cases	Insulin Test: Positive	Insulin Test: Negative	Insulin Test: Unsatisfactory	Proof
Duodenal ulcer					
Vagotomy alone	2	1	..	1	Ulcer proved by operation elsewhere in 1, at clinic in 1
Gastroenterostomy	3*	..	3	..	Roentgenologic and surgical evidence of gastrojejunal ulcer in 3; roentgenologic evidence in 2
	2†	1†	..	..	
Gastrojejunal ulcer after gastroenterostomy					
Vagotomy alone	1	..	1	..	Roentgenologic and surgical evidence of gastrojejunal ulcer in 1 yr.
Gastroenterostomy removed, gastroduodenal continuity established	2	..	2	..	Duodenal ulcer on roentgenologic examination in both
Gastrojejunal ulcer after gastric resection					
Vagotomy alone	3	1†	1†	..	Roentgenologic and surgical evidence in all cases
Gastric ulcer					
Vagotomy alone	2	..	2	..	Gastric ulcer recurred; roentgenologic and surgical proof
	1†	1†	..	..	
Total Series 1	10	1	8	1	
Series 2	6	3	1	0	

* One patient underwent enteroanastomosis.
† Series 2.

studies and 46 were followed by questionnaire one to four years after operation. In this series likewise there were three hospital deaths. There were six proved (table 2) and eight suspected (table 3) recurrences of ulcer. In order to contrast groups of cases in which a series of personal observations and studies were made

with those in which contact was made with the patient by mail, it was thought worth while to contrast these results with those reported in 2,558 collected cases [3] before the American Gastroenterological Association [4] at their 1950 meeting by Dr. Sara Jordan, Chairman of their Vagotomy Committee. In the physiologic studies to be reported in this paper, the results are obtained from cases in series 1 alone (87 cases) because follow-up studies were planned with this study in mind whereas such was not the case in series 2, in which the postoperative physiologic studies on returning patients were too scanty and made in too few cases to contrast them with results of physiologic studies in series 1. However, a comparison of subjective and objective clinical results can be made in series 1, 2 and 3.

THE EFFECT OF GASTRIC VAGOTOMY ON GASTRIC ACIDITY

This effect can best be determined in cases in which the operation has been done in the treatment of duodenal or gastric ulcer for which no other procedure, such as gastroenterostomy, pyloroplasty or gastric resection, has been done simul-

TABLE 3.—*Suspected Recurrence in Series 1 and 2*

Ulcer and Associated Operation	Cases	Insulin Test: Positive	Insulin Test: Negative	Insulin Test: Unsatisfactory	Proof
Duodenal ulcer	1	..	..	1	Pain in 1; hemorrhage in 1
Vagotomy alone	1*	..	..	1*	
With gastroenterostomy	1	..	..	..	Ulcer pain in 3; hemorrhage in 1, all within 1 yr. after operation
	2*	..	1*	..	
Gastrojejunal ulcer after gastroenterostomy	1	..	1	..	Pain 12, 12, 13, 24 mo. after operation; 5 hemorrhages in 1 case
Vagotomy alone	3*	1*	..	1*	
Gastrojejunal ulcer after gastric resection	1	..	..	1	Pain began 6 mo., 6 mo. and 1 yr. after operation
Vagotomy alone	2*	..	..	..	
Total Series 1	4	..	1	2	
Series 2	6	1	1	2	

* Series 2.

taneously or previously which, by removal of part of the stomach or an increase in the intragastric flow of duodenal content, would reduce or dilute gastric secretions by causing the entrance of alkaline intestinal secretion into the stomach. There is a group of cases, however, in which valuable information can be obtained and that is those in which gastrojejunal ulcer develops after gastroenterostomy or gastric resection. In such cases the reduction of gastric acidity following vagotomy can be determined by comparison of the gastric acidity before and after operation.

The gastric acidity was determined in all cases after the Ewald test meal. Histamine was used in only a few cases, and the results are not reported in this study. Tests of night secretion were performed in the immediate postoperative period in many cases, but owing to the inconvenience to the patient they were not performed before operation or at the time of the follow-up visit. Thus these results will not be reported in this paper. Determinations of free hydrochloric acid in the

3. These cases were collected with the cooperation of 28 surgeons in 12 cities who had performed 50 or more operations. Individual case reports were sent to the Vagotomy Committee by each surgeon.

4. Report of Subcommittee on Vagotomy for Peptic Ulcer, presented before the Fifty-First Annual Meeting of the American Gastroenterological Association, Atlantic City, April 29, 1950.

stomach were made on the ninth to the twentieth postoperative day in 31 cases in which vagotomy was performed alone for duodenal ulcer and gastric ulcer in which no previous operation had been performed on the stomach. In 93.5 per cent acidity was reduced when compared with the preoperative level; in 38.7 per cent there was relative achlorhydria. In the follow-up group, studies were made after one to four years on 22 patients; 76.3 per cent had a reduction of free hydrochloric acid in the gastric contents, including the 27.3 per cent who had relative achlorhydria. The free hydrochloric acid of 23.7 per cent had returned to preoperative levels.

Of the 12 patients with gastrojejunal ulcer after gastroenterostomy, one had achlorhydria before vagotomy. After vagotomy alone was performed achlorhydria was obtained in seven (58.3 per cent). A postoperative reduction in the hydrochloric acid level occurred in an additional 25 per cent, and no reduction occurred in 16.7 per cent (patient who had achlorhydria before vagotomy included with the seven). Unfortunately, however, all three patients available for study one to

TABLE 4.—*Gastric Free Hydrochloric Acid, Series 1*

Vagotomy	Cases Studied		Absent, Per Cent of Cases*		Reduced, Per Cent of Cases*		No Change, Per Cent of Cases*	
	Immediate†	Late‡	Immediate†	Late‡	Immediate†	Late‡	Immediate†	Late‡
Alone								
No previous gastroenterostomy or gastric resection	31	22	38.7	26.3	54.8	50.0	6.5	23.7
Gastroenterostomy previously	12	3	58.3	66.7	25.0	33.3	16.7	0
Gastric resection previously	14	8	100.0	100.0	0	0	0	0
Combined with								
Gastroenterostomy	54	29	42.3	24.1	49.2	65.6	7.5	10.3
Gastric resection	14	11	84.7	80.8	7.6	9.6	7.6	9.6
Pyloroplasty	8	7	87.5	71.4	12.5	28.6	0	0
Gastroenteric anastomosis taken down	5	5	20.0	0	20.0	40.0	60.0	60.0

* Per cent of cases in each group.
† Studies made in 138 cases.
‡ Studies made in 85 cases

four years after vagotomy showed reduction of gastric acidity, two of these to an achlorhydric level.

There were 14 cases of gastrojejunal ulcer after previous gastric resection; in seven achlorhydria was present before vagotomy, and in the remaining seven relative achlorhydria developed after vagotomy. We have been able to study only eight of these patients one year or longer after operation; all have continued to have achlorhydria.

When vagotomy is combined simultaneously with gastroenterostomy or gastric resection, the immediate and late results, as can be seen from table 4, closely parallel those in which these associated procedures were performed previous to the vagotomy.

THE EFFECT OF GASTRIC VAGOTOMY ON GASTRIC MOTILITY

Gastric motility in patients may be measured by two methods: (1) the balloon photokymographic method and (2) the roentgenoscopic and roentgenographic method. The former method measures changes in motility quantitatively. High-

tower and Code,[5] of the Mayo Clinic, have adapted the terminology of Templeton and Lawson,[6] Adler, Atkinson and Ivy[7] to motility waves observed in gastric motility records. They have studied 15 vagotomized patients in a period ranging from three weeks to nine months after operation and have found that the type II wave ("hunger contraction") is decreased in amount as well as in amplitude. They have found that urethane of β-methylcholine chloride (urecholine®) in a 5.0 mg. dose given subcutaneously counteracts temporarily the changes produced by vagotomy.

The roentgenoscopic method of studying motility varies with the roentgenologist and is subject to personal error, as contrasted with the kymographic balloon studies. However, when correlated with studies of roentgenograms it furnishes valuable information, and any roentgenologist can carry it out. Roentgenoscopic and roentgenographic studies were made in 99 cases in series 1 nine to 20 days after operation. This method was used as it was more readily available (table 5).

TABLE 5.—*Gastric Motility, Series 1*

Vagotomy	Cases Studied		Absent, Per Cent*		Reduced, Per Cent*		Normal, Per Cent*	
	Immediate†	Late‡	Immediate†	Late‡	Immediate†	Late‡	Immediate†	Late‡
Alone								
No previous gastroenterostomy or gastric resection	26	19	65.3	28.4	7.6	0	27.1	73.6
Gastroenterostomy or gastric resection previously	17	14	41.1	....	11.7	....	47.2	100.0
Combined with								
Gastroenterostomy	28	24	56.0	0	12.0	....	32.0	100.0
Gastric resection	14	11	14.4	9.6	7.1	....	78.5	90.4
Pyloroplasty	10	6	50.0	16.7	12.5	16.7	37.5	66.6
Gastroenteric anastomosis taken down	4	5	25.0	0	25.0	20.0	50.0	80.0

* Per cent of cases in each group.
† Studies made in 99 cases.
‡ Studies made in 79 cases.

Gastric motility was relatively absent in about 50 per cent of the cases at this time, that is, a large dilated stomach was described, with no evidence of peristaltic activity. Motility was decreased in an additional 15.5 per cent but was normal in about 34 per cent of the cases. Motility was studied in 26 cases of duodenal and gastric ulceration in which vagotomy alone was performed without associated operations at the same time or previously. Relative gastric motility was absent in 65.3 per cent, decreased in 7.6 per cent and normal in 27.1 per cent. Of the 17 patients in whom previous gastroenterostomy or gastric resection had been done and vagotomy alone was performed, 41.1 per cent showed atony, 11.7 per cent showed decreased motility and 47.2 per cent showed normal motility. Of 28 patients who underwent vagotomy and gastroenterostomy simultaneously, 56 per cent had atony, 12 per cent decreased motility and 32 per cent normal motility.

5. Hightower, N. C., and Code, C. F.: Personal communication to the authors.

6. Templeton, R. D., and Lawson, H.: Studies in the Motor Activities of the Large Intestine: I. Normal Motility in the Dog, Recorded by the Tandem Balloon Method, Am. J. Physiol. **96**:667-676 (March) 1931.

7. Adler, H. F.; Atkinson, A. J., and Ivy, A. C.: A Study of the Motility of the Human Colon: An Explanation of Dysynergia of the Colon, or of the "Unstable Colon," Am. J. Digest. Dis. **8**:197-202 (June) 1941.

Of 10 patients on whom vagotomy and pyloroplasty were done simultaneously, 50 per cent had atony, 12.5 per cent decreased motility and 37.5 per cent normal motility. Of the 14 patients who underwent simultaneous vagotomy and gastric resection, 14.4 per cent had atony, 7.1 per cent decreased motility and 78.5 per cent normal motility.

These results show the reduction in the loss of gastric motility when a gastric drainage operation is performed previous to the vagotomy, especially striking when gastric resection decreases the size of the secreting gastric surface and provides a maximal degree of drainage of what remains of the gastric secretion or what is taken into the stomach. In four cases of gastrojejunal ulcer in which vagotomy was performed the gastroenteric anastomosis was removed and gastroduodenal continuity was reestablished by closure of the openings in the jejunum and stomach. Motility was absent in 25 per cent, decreased in 25 per cent and normal in 50 per cent.

Follow-up data were obtained in 79 cases covering a period of 18 months to four years. Relative gastric motility had returned in 83.6 per cent of cases. However, it was still absent in 3.8 per cent and decreased in 12.5 per cent. Motility studies were done in this late period in 19 cases of duodenal or gastric ulcer in which vagotomy alone, without any associated or previous operation on the stomach, was performed. Motility had returned in 73.6 per cent of cases but was below normal, with persisting dilatation, in five (26.4 per cent). However, motility was absent or decreased in only 3.6 per cent of the cases in which vagotomy was combined with simultaneous or previously performed gastroenterostomy, pyloroplasty or gastric resection (table 5).

In this late follow-up study the advantages of associated operations on the stomach which assist in its emptying is apparent in promoting the return of gastric motility.

INSULIN TESTS OF INTERRUPTION OF GASTRIC VAGAL NERVE

Review of the literature has shown a diversity of opinion as to the value of the insulin test in evaluating the completeness of gastric vagal nerve resection. Weinstein, Hollander, Lauber and Colp [8] came to the conclusion that the insulin test could not be used as an indication of the clinical results of vagotomy. Our experience showed that there was a good (about 80 per cent) correlation of negative insulin reactions with excellent clinical results. With the disparity between these conclusions in mind, we reviewed the methods of performing insulin tests used by ourselves and by Hollander and his associates and concluded, as he did, that the reason for the difference in correlation of results might be due to the differences in the manner of performing and interpreting the tests. However, we have found on reviewing the insulin reactions obtained in our cases with poor results (proved recurrence of ulcer) that the correlation with clinical results was only good in 23.1 per cent of the 16 cases. Insulin tests gave negative results in 10, positive results in three and unsatisfactory results (or tests were not done) in three cases. This would indicate that while the insulin reaction appears to be a good prognostic sign

8. Weinstein, V. A.; Hollander, F.; Lauber, F. U., and Colp, R.: Correlation of Insulin Test Studies and Clinical Results in a Series of Peptic Ulcer Cases Treated by Vagotomy, Gastroenterology **14**:214-227 (Feb.) 1950.

in an over-all group of cases it is of little value in that most important group, the one in which there are recurrences.

It has been the custom at the Mayo Clinic to perform insulin tests in the following manner: The fasting patient has his stomach aspirated, and blood is withdrawn for a determination of the sugar level. Then 0.3 unit of regular insulin per kilogram of body weight is injected intravenously and aspiration of gastric contents and withdrawal of blood for sugar determination are done simultaneously every 15 minutes for five times after the injection of insulin. The tests are interpreted in the following manner: When the blood sugar is not decreased to 35 mg. per 100 cc. or less, the test is declared unsatisfactory. When the depression of the blood sugar has been satisfactory, the result of the test is considered to be negative if the free acids (in the stomach contents withdrawn simultaneously with each specimen of blood for the determination of blood sugar) are depressed to their lowest level and do not show a rise at the point of greatest hypoglycemia.

TABLE 6.—*Insulin Response After Vagotomy: Results of Insulin Tests Evaluated According to Criteria of Weinstein, Hollander, Lauber and Colp* [8]

Operation	Workers	Results of Test					
		Negative	Positive	Equivocal	Antacid	Inadequate	Total
Duodenal ulcer							
Vagotomy alone	Weinstein and co-workers	12 (60%)	8 (40%)	0 (0%)	0 (0%)	0 (0%)	20*
	Mayo Clinic, series 1.....	17 (85%)	.....	1 (5%)	1 (5%)	1 (5%)	20
Vagotomy with gastroenterostomy	Weinstein and co-workers	11 (39%)	12 (43%)	1 (4%)	4 (14%)	.....	28
	Mayo Clinic, series 1.....	32 (71%)	3 (6%)	.....	9 (20%)	1 (3%)	45
Vagotomy with gastric resection	Weinstein and co-workers	12 (21%)	7 (12%)	2 (3%)	37 (64%)	.....	58
	Mayo Clinic, series 1.....	1 (12%)	.....	.....	5 (63%)	2 (25%)	8
Vagotomy and pyloroplasty	Mayo Clinic, series 1.....	5 (83%)	.....	.....	1 (17%)	.....	6
Gastrojejunal ulcer							
Vagotomy	Weinstein and co-workers	1 (5%)	9 (47%)	1 (5%)	8 (42%)	.....	19
Vagotomy after gastroenterostomy	Mayo Clinic, series 1.....	8 (62%)	.....	.....	5 (38%)	.....	13
Vagotomy after gastric resection	Mayo Clinic, series 1.....	1 (8%)	.....	.....	11 (92%)	.....	12

* One gastric ulcer included.

If there is a rise in the free acids when the greatest hypoglycemia is attained, the result of the test is considered to be positive.

Hollander and his associates differ in their criteria for results in several particulars: 1. A concentration of blood sugar of 50 mg. per 100 cc. is considered to indicate adequate hypoglycemia. 2. An increase of 10 mN (clinical units) from an acid base line or of 20 mN from the average of two fasting specimens if these are not antacid is considered to give a negative result. 3. Five groups, positive, negative, achlorhydric, equivocal and inadequate, are used in interpreting results in contrast to our three groups, positive, negative and unsatisfactory.

It is reasonable to suppose that there would be discrepancies between results reported from insulin tests performed by each group. In an effort to make a comparison between the results of the tests, it was decided to arrange our data according to the criteria established by Weinstein, Hollander, Lauber and Colp [8] and to see if an insight might be gained into the differences in the results of insulin tests performed by various investigators. Accordingly, the results of insulin tests in 104 comparable cases in which vagotomy was performed by one of us (Walters) were interpreted according to the other criteria and arranged in tables similar to those of Weinstein, Hollander, Lauber and Colp, together with the data on 125

cases in which insulin tests had been performed and reported by them (tables 6, 7 and 8). There is a higher incidence of negative results of insulin tests and a

TABLE 7.—*Response to Insulin Test on Follow-up Compared with Early Postvagotomy Response: Tests Interpreted According to Criteria of Weinstein, Hollander, Lauber and Colp* [8]

Early			Late		
	Series				
Result of Test	Weinstein and Co-Workers	Mayo Clinic, Series 1	Types of Response	Weinstein and Co-Workers	Mayo Clinic, Series 1
Negative	37	64	Negative	11	24
			Positive	5	5
			Equivocal	0	0
			Antacid	1	0
			No adequate test	20	3 (32 not repeated)
Positive	25	3	Negative	0	0
			Positive	5	3
			Equivocal	1	0
			Antacid	3	0
			No adequate test	16	0
Equivocal	5	1	Negative	0	0
			Positive	1	0
			Equivocal	2	0
			Antacid	0	0
			No adequate test	2	1
Antacid	43	32	Negative	1	1
			Positive	0	0
			Equivocal	0	0
			Antacid	8	7
			No adequate test	34	0 (24 not repeated)
No adequate test	15	4	Negative	3	4
			Positive	6	0
			Equivocal	0	0
			Antacid	6	0

TABLE 8.—*Comparison of Clinical Results of Vagotomy Alone for Duodenal Ulcer Correlated with Insulin Tests Evaluated on the Criteria of Weinstein, Hollander, Lauber and Colp* [8]

			Ulcer			Motility Effects		
Postvagotomy Insulin Test	Result		Healed	Recurrent	Persistent	Severe	Moderate	Diarrhea
Weinstein and co-workers	Positive	8	6 (75%)	2 (25%)	0 (0%)	3 (38%)	5 (63%)	2 (25%)
	Negative	12	9 (75%)	2 (17%)	1 (8%)	2 (17%)	8 (67%)	3 (25%)
Mayo Clinic, series 1	Positive	5	4 (80%)	1 (20%)	.....	2 (40%)	.....	.....
	Negative	17	12 (71%)	1 (6%)	4 (23%)*	3 (18%)	7 (41%)	4 (24%)

* Roentgenologic reports of duodenal deformity.

lower incidence of positive results than we encountered when the tests were interpreted according to our criteria (tables 9 and 10). By their criteria there is a much smaller number of tests which are labeled "no adequate test" or, in our terms, "unsatisfactory" than was seen when the data were interpreted according to our criteria. The results of the insulin tests repeated by us in the one to four year postvagotomy period are comparable to those found by Weinstein, Hollander, Lauber and Colp.

The clinical correlation of the results of the insulin tests of vagotomy alone for duodenal ulcer are presented in table 8 according to the criteria of Weinstein and

TABLE 9.—*Results of Insulin Tests After Operations in Series 1*

Operation	Cases	Type of Result	Immediate Results	Correlation of Clinical Results with Results of Late Insulin Test		
				Excellent	Unsatisfactory	Poor
For duodenal ulcer						
Vagotomy alone	22	Negative	12	8	3	1
		Positive	1	3	1	1
		Unsatisfactory	8	1	2	1
Vagotomy and gastroenterostomy	51	Negative	22	30	1	1
		Positive	2	4	1	5
		Unsatisfactory	17	1	1	..
Vagotomy and gastric resection	8	Negative	2	3	..	..
		Positive	..	..	..	..
		Unsatisfactory	6	..	..	..
Vagotomy and pyloroplasty	6	Negative	4	3	..	1
		Positive	1	1	..	..
		Unsatisfactory	..	..	..	..
For gastrojejunal ulcer						
Vagotomy after gastroenterostomy	12	Negative	8	6	..	2
		Positive	2	1	..	1
		Unsatisfactory	2	1	..	1
Vagotomy after gastric resection	14	Negative	11	10	..	1
		Positive	..	..	..	2
		Unsatisfactory	3	..	1	..
For gastric ulcer	10	Negative	4	3	1	..
		Positive	1	1	..	..
		Unsatisfactory	..	..	..	..

TABLE 10.—*Results of Insulin Tests Performed After One Year in Series 1*

Operation	Unsatisfactory Tests Which Changed		Satisfactory Tests Which Changed		Number of Tests		
			Positive to	Negative to			
	Negative	Positive	Negative	Positive	Negative	Positive	Unsatisfactory
For duodenal ulcer							
Vagotomy alone	1	3	..	2	6	4	2
Vagotomy and gastroenterostomy	6	3	..	..	32	3	..
Vagotomy and pyloroplasty	..	..	1	..	9	..	..
For gastrojejunal ulcer after gastroenterostomy	..	..	1	1	3	1	..
For gastrojejunal ulcer after gastric resection	..	..	..	..	5	..	..
For gastric ulcer	4	1	1	1	11	2	..

his associates. The inference which may be drawn is that with more stringent criteria for a positive insulin test the results may form a more dependable basis for prognosticating the results of vagotomy for peptic ulcer. Tables 9 and 10 are

used to show the results of the insulin tests interpreted according to our criteria correlated with the long term clinical results.

PHYSIOLOGIC RESULTS IN POSTERIOR VAGAL NERVE SECTION ONLY

McSwiney [9] and numerous other investigators have shown that only the posterior vagus trunk innervates the pylorus and that the anterior vagus trunks send no nerve filaments to this region. Gregory and Ivy [10] have shown that gastrin is elaborated by vagal stimulation of the cells in the pyloric area. From these studies has come the theory that if the posterior vagus nerve is divided a reduction in gastric acidity should occur in all cases.

Since the question has arisen as to whether it is possible to divide all the vagus nerves to the stomach and since there seems to be some inconsistencies in the reasoning that a negative result from insulin tests shows that all nerves are divided, we thought it a good plan to divide and resect only one of the main branches of the vagus in association with an operation such as gastroenterostomy or gastric resection, which of themselves heal or remove the ulcer and reduce gastric acidity. The larger branch, namely, the posterior one, was divided as a supplementary procedure to gastroenterostomy in six cases and as supplementary to gastric resection in a seventh.

The insulin test gave a negative result in four of these cases, was unsatisfactory in two and unfortunately was not done in one. An interesting corollary of this was that three patients (one with a negative insulin reaction) who had undergone gastroenterostomy with section of a single vagus had postoperative achlorhydria. Achlorhydria will occur after gastroenterostomy without vagotomy in 12 per cent of cases. The fact that the patient who had undergone vagotomy of one trunk and gastric resection had achlorhydria is without significance, for 72 per cent of patients have relative achlorhydria after adequate partial gastrectomy.

Five of these patients returned one to four years after operation for examination. The insulin test on three gave negative results and was not done on two. Six months after operation, a recurring ulcer developed in one of the six patients who had undergone gastroenterostomy and resection of a single vagus nerve and gave a negative reaction to the insulin test.

CLASSIFICATION OF THE EFFECTS OF VAGOTOMY ON VARIOUS TYPES OF PEPTIC ULCER (TABLES 11, 12 AND 13)

Results in the follow-up studies in all series have been classified in three categories: The result is considered (1) excellent when the patient is completely relieved of symptoms of ulcer and has no symptoms relating to vagotomy, such as diarrhea, gastric retention or bloating, (2) unsatisfactory when the patient has no evidence of recurrence of ulcer but has troublesome symptoms directly related to vagotomy, such as diarrhea, gastric retention and bloating, or has symptoms suggestive of ulcer but recurrence has not been proved, and (3) poor when recurrence of ulcer has been proved.

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9. McSwiney, B. A.: Innervation of the Stomach, Physiol. Rev. **11**(pt. 1):478-514 (Oct.) 1931.

10. Gregory, R. A., and Ivy, A. C.: The Humoral Stimulation of Gastric Secretion, Quart. J. Exper. Physiol. **31**:111-128, 1941.

TABLE 11.—*Clinical Results of Duodenal Ulcer in Series 1*, 2* and 3†*

Vagotomy	Series	Cases	Percentage of Cases				
			Excellent Results	Unsatisfactory Results	Symptoms of Ulcer		Poor Results
					No	Yes	
Alone	1	21	57.2	33.3	90.5	9.5	9.5
	2	8	75.0	25.0	100.0	0	0
	3	728	75.6	18.4	87.0	13.0	6.0
With gastroenterostomy	1	37	75.7	16.2	84.0	16.0	8.1
	2	44	86.4	9.1	87.0	13.0	4.5
	3	1,046	93.2	5.3	98.2	1.8	1.5
With gastric resection	1	8	62.5	37.5	100.0	0	0
	2	1	....	100.0	100.0	0	0
	3	353	85.9	11.3	92.4	7.6	2.8
With pyloroplasty	1	6	66.7	33.3	100.0	0	0
	2	3	33.3	66.7	100.0	0	0
	3	114	84.4	11.2	92.0	8.0	4.4

* Mayo Clinic.
† Collected series of American Gastroenterological Association.

TABLE 12.—*Clinical Results of Gastrojejunal and Gastroduodenal Ulcer in Series 1*, 2* and 3†*

Lesion and Operation	Series	Cases	Percentage of Cases				
			Excellent Results	Unsatisfactory Results	Symptoms of Ulcer		Poor Results
					No	Yes	
Gastrojejunal ulcer after gastroenterostomy							
Vagotomy alone	1	8	62.5	25.0	75.0	25.0	12.5
	2	12	75.0	25.0	75.0	25.0	0
Vagotomy and gastroenteric anastomosis taken down	1	4	50.0	0	50.0	50.0	50.0
	2	1	100.0	0	100.0	0	0
Gastrojejunal ulcer after gastric resection							
Vagotomy alone	1	11	72.8	27.2	91.6	8.4	0
	2	18	61.1	22.2	77.3	22.7	16.7
Vagotomy and gastric resection	1	3	66.7	33.3	100.0	0	0
Gastroduodenal ulcer after Billroth I							
Vagotomy alone	1	1	100.0	....	100.0	0	0
Vagotomy and gastric resection	1	2	100.0	....	100.0	0	0

* Mayo Clinic.
† Collected series of American Gastroenterological Association. Note: 250 patients in series 3 underwent vagotomy for gastrojejunal ulcer. No distinction was made as to whether gastrojejunal ulcer occurred after gastroenterostomy or gastric resection. Follow-up data revealed excellent results in 83.1 per cent, proved recurrence of ulcer in 9.5 per cent and unsatisfactory results in 7.4 per cent.

TABLE 13.—*Clinical Results of Gastric Ulcer in Series 1*, 2* and 3†*

Vagotomy	Series	Cases	Percentage of Cases				
			Excellent Results	Unsatisfactory Results	Symptoms of Ulcer		Poor Results
					No	Yes	
Alone	1	9	22.2	55.5	77.8	22.7	22.2
	2	2	50.0	....	50.0	50.0	50.0
	3	..	....	....	....	....	....
With gastroenterostomy	1	2	100.0	....	100.0	0	0
	2	..	....	....	....	....	....
	3	..	....	....	....	....	....
With gastric resection	1	..	....	....	....	....	....
	2	..	....	....	....	....	....
	3	54	89.5	10.5	95.0	5.0	0

* Mayo Clinic.
† Collected series of American Gastroenterological Association.

RESULTS OF VAGOTOMY ALONE

Duodenal Ulcer.—Series 1: Vagotomy alone was performed in 24 cases of duodenal ulcer in series 1. Two patients died in the immediate postoperative period, one of coronary occlusion and the other of uremia. One died at home 11 months postoperatively of volvulus and gangrene of the terminal portion of the ileum. Eighteen patients returned for reexamination. Of these, 10 (55.5 per cent) had excellent results. Two additional patients were considered to have excellent results by their replies to questionnaires. Six of the reexamined patients had unsatisfactory results, two had poor results, with proved recurring duodenal ulcer, and one had (by questionnaire) suspected recurrence of duodenal ulcer 18 months after operation as evidenced by severe recurrent pain. One interesting patient in the unsatisfactory group had a pronounced disturbance of motility three and a half years after vagotomy alone was performed for duodenal ulcer. Pyloroplasty was later performed, at which time no evidence of duodenal ulcer was found. A summary of these results in the examined and questionnaire groups shows that they were excellent in 12 (57.2 per cent), unsatisfactory in seven (33.3 per cent) and poor in two (9.5 per cent).

Series 2: In series 2 of 15 patients operated on, two patients died in the immediate postoperative period, one from perforation of duodenal ulcer with a subphrenic abscess and the other from uremia. Of the 13 remaining patients, seven had one to four year follow-up by examination and laboratory studies. The results were excellent in six (57.1 per cent) and unsatisfactory in one (42.9 per cent). One additional patient who reported by questionnaire had symptoms of moderate gastric retention.

Series 3: In series 3 there were 728 patients who underwent vagotomy alone for duodenal ulcer, with an average follow-up of one and a half to two years; 75.6 per cent had excellent, 18.4 per cent unsatisfactory and 6.0 per cent poor results or recurrent ulcers.

Gastric Ulcer.—Series 1: Vagotomy alone was performed for gastric ulcer in 10 cases, series 1. The reason for such a small group is that we believe partial gastrectomy is an ideal operation for this lesion, which has at least a 20 per cent chance of being unsuspectedly malignant. Examination and laboratory studies were made one to four years after operation in nine cases, with excellent results in two (22.2 per cent) and unsatisfactory results in five (55.5 per cent). In two of these five there was evidence of persistence of gastritis on gastroscopic examinations, although both patients were free of symptoms and one had gained 20 to 30 pounds (9.1 to 13.6 Kg.), and in the other three cases in which results were unsatisfactory troublesome postvagotomy symptoms were present. Poor results were found in two cases (22.2 per cent). Both patients were found by roentgenogram and at operation to have large recurrent gastric ulcers for which gastric resections were done, with excellent results.

Series 2: In series 2 only two patients returned for examination and laboratory studies; one had excellent results and one had a recurrence in one year.

Series 3: Vagotomy was associated with gastric resection in all cases of gastric ulcer. Thus, comparable figures are not available for this group of cases.

Gastrojejunal Ulcer After Gastroenterostomy.—Series 1: Vagotomy was performed for gastrojejunal ulcer after gastroenterostomy in 14 cases in series 1. Examination was made in five cases one to four years after operation, with excellent results in three, unsatisfactory in one and a recurrent gastrojejunal ulcer in one. Three additional patients replied to questionnaires. Two were interpreted as having excellent results, but one had an unsatisfactory result, with a return of ulcer symptoms. One patient had severe recurrent pain and diarrhea one year after operation. Thus in this group of eight patients followed, the results were excellent in five, unsatisfactory in two and poor in one. The last patient had a recurrence of the gastrojejunal ulcer six months after operation, for which gastric resection was performed.

Series 2: There were 24 cases in this group. A follow-up of one year or longer was carried out in 12 cases, in nine of which results were excellent and in three unsatisfactory. However, of this group only two patients returned for reexamination one to four years after operation. Both had excellent results. The three patients in the unsatisfactory group reported by questionnaire, and a recurrence of ulceration was suspected but was not proved.

Series 3: In series 3, 250 cases of gastrojejunal ulcer were reported, with no distinction as to whether ulceration was present after gastric resection or after gastroenterostomy. However, results were reported as excellent in 83.1 per cent, unsatisfactory in 7.4 per cent and poor in 9.5 per cent.

Gastrojejunal and Gastroduodenal Ulcer After Gastric Resection.—Gastrojejunal Ulcer, Series 1: In series 1, 14 patients who had gastrojejunal ulcer after gastric resection were treated by vagotomy alone; follow-up data were available on 11 one to four years after operation. Six of these patients returned for examination, and results were excellent in five and unsatisfactory in one. The results, obtained by questionnaire in five additional cases, were excellent in three and unsatisfactory in two. One of the latter patients stated in a letter a year after operation that he had severe recurrent pain and gastric retention but no recurrent ulceration had been proved. A summary of the results in this group shows that eight (71.8 per cent) patients had excellent results and three (27.2 per cent) had unsatisfactory results. One of the patients who had an unsatisfactory result lived in Iceland, and a recurrence of the gastrojejunal ulcer was suspected one year after operation.

Gastrojejunal Ulcer, Series 2: One to four year follow-up data were obtained in 18 cases; results were excellent in 11 (61.1 per cent), unsatisfactory in four (22.2 per cent) and poor in three (16.7 per cent). However, only 10 of these patients returned for examination, of whom six showed excellent results, one an unsatisfactory result and three a poor result.

Gastroduodenal Ulcer, Series 1: There was one patient in series 1 who had a gastroduodenal ulcer after a Billroth I gastric resection for which vagotomy alone was performed. Results were excellent, as proved by examination 18 months after operation.

Gastrojejunal Ulcer, Series 3: The results have been discussed previously, since no distinction was made between gastrojejunal ulcer after gastroenterostomy and after gastric resection.

VAGOTOMY PLUS GASTROENTEROSTOMY

Series 1.—Vagotomy plus gastroenterostomy has been performed in 54 cases in series 1, in 52 for duodenal ulcer and in 2 for gastric ulcer. Twenty-seven patients on whom this operation was performed for duodenal ulcer returned for examination one to four years after operation; 20 (74.0 per cent) had excellent results, four (14.9 per cent) unsatisfactory results and three (11.1 per cent) poor results. Of the 10 additional patients followed by questionnaire, eight (80 per cent) had excellent results and two (20 per cent) unsatisfactory results, with one patient reporting that a severe gastrointestinal hemorrhage occurred 16 months after operation, but there was no proved recurrence of ulcer. Of the three patients who had poor results after this operation for duodenal ulcer, gastrojejunal ulcer developed in one, reported on previously.[2c] The second patient had a recurrence of ulcer distress 18 months after operation, at which time the roentgenograms showed evidence of gastrojejunitis. A gastrojejunal ulcer was found at operation, and gastric resection was performed. (The patient had a negative insulin reaction immediately after operation, but unfortunately no insulin test was done at 18 months after operation.) The third patient had symptoms of ulcer 14 months after operation. Roentgenograms showed evidence of gastrojejunitis which improved somewhat under medical management. (The immediate postoperative insulin test was unsatisfactory, and that made 18 months after operation gave positive results.)

Ten patients (19.2 per cent) had gastric retention postoperatively necessitating prolonged hospitalization (29 days average).

In summary of this group of cases in which vagotomy and gastroenterostomy were performed, 75.7 per cent of the patients showed excellent results, 16.2 per cent showed unsatisfactory results and 8.1 per cent showed proved or suspected gastrojejunal ulceration. In the two cases in which vagotomy plus gastroenterostomy was performed by one of us (Walters) for gastric ulcer, results were excellent 18 months after operation. One patient showed healing of the gastric ulcer by roentgenologic examination, and the other reported complete relief of symptoms by questionnaire.

Series 2 (109 Cases).—Of this group, 44 patients on whom the operation was done for duodenal ulcer were followed one year or longer. Thirty-eight (86.4 per cent) reported excellent results, four (9.1 per cent) had proved or suspected recurrence of ulcer and two had reported prolonged motility disturbances. However, only 17 of these patients returned for examination, of whom 13 (76.4 per cent) showed excellent results, two (11.8 per cent) unsatisfactory results and two (11.8 per cent) poor results. No follow-up data were available after operations of this nature for gastric ulcer in series 2.

Series 3.—Results in the 1,046 cases studied over one year were excellent in 93.2 per cent, unsatisfactory in 5.3 per cent and poor in 1.5 per cent. It was not stated whether this information was obtained by personal examination and laboratory study or by questionnaire. Our experience as indicated later in this paper indicates that results obtained by questionnaire are uniformly better than those acquired from reexamination of the patients.

VAGOTOMY PLUS PYLOROPLASTY

Series 1.—Vagotomy plus pyloroplasty was performed in six cases for duodenal ulcer. In all six cases the patients were followed more than one year by examination and laboratory studies, and excellent results were obtained in four and unsatisfactory results in two. There were no known recurrences of ulcer.

Series 2.—In three cases vagotomy was combined with pyloroplasty for duodenal ulcer, with follow-up data for one to four years. One patient had an excellent result, and two had disturbances of motility in the third and fourth years which were not severe enough to warrant further surgical treatment.

Series 3.—Follow-up data were available in 114 cases one and one-half to two years after operation. In 84.4 per cent results were excellent, in 11.2 per cent unsatisfactory and in 4.4 per cent poor.

VAGOTOMY PLUS GASTRIC RESECTION

Series 1.—Vagotomy combined with gastric resection was performed in 14 cases, in 12 of which follow-up data were obtained one to four years later. Eight patients who had duodenal ulcer returned for examination. Five had excellent results (62.5 per cent) and three (37.5 per cent) unsatisfactory results, owing to the dumping syndrome in one and to troublesome epigastric fulness in two. No recurrent ulcers were found in this group.

Five patients underwent vagotomy and gastric resection for gastrojejunal ulcer after inadequate gastric resection. One patient in this group died on the twenty-sixth postoperative day of uremia secondary to a perforation of a loop of jejunum just below the anastomosis from volvulus. Of three who replied to questionnaires, two had excellent results and one unsatisfactory results.

Two patients who had gastroduodenal ulcer after a Billroth I gastric resection showed excellent results on examination 18 and 24 months after vagotomy and a second gastric resection.

Series 2.—In this group one patient only who underwent gastric resection combined with vagotomy for duodenal ulcer was followed for more than one year by examination. There was no recurrence, but the patient exhibited moderate gastric retention.

Series 3 (407 Cases).—In 353 cases in this series vagotomy was combined with gastric resection for duodenal ulcer. Results were excellent in 85.9 per cent, unsatisfactory in 11.3 per cent and poor in 2.8 per cent. Excellent results were obtained in 89.5 per cent of the 54 cases of gastric ulcer in which this operation was performed and unsatisfactory results in 10.5 per cent, and no poor results were reported.

REMOVAL OF GASTROJEJUNAL ANASTOMOSIS FOR GASTROJEJUNAL ULCER WITH RESTORATION OF GASTROINTESTINAL CONTINUITY AND VAGOTOMY

Series 1.—This procedure was performed in five cases in series 1. Four patients returned for examination one year or longer after operation. Two patients (50 per cent) had poor results, confirmed in both by roentgenologic demonstration of

a recurrence of an active duodenal ulcer, one in 14 months and the other in 42 months after operation. No further operation has been done on either of these patients to date. The other two patients showed excellent results in three years, with no evidence of active duodenal ulcer on roentgenologic examination.

Series 2.—In one case in series 2 in which this procedure was performed, follow-up data were available; results were excellent in this case.

Series 3.—No statistics are available for this group of cases.

EFFECTS OF VAGOTOMY ON PEPTIC ULCERATION

Let us consider the questions raised in the evaluation of what vagotomy does in the human being with peptic ulcer. First, we will consider its effect on gastric acidity and motility and how long this effect lasts. It does reduce gastric motility and does produce dilatation of the stomach in most cases, but motility returns to the stomach, and the stomach returns to a size reasonably comparable with what it was before vagotomy in most but not all cases within 18 months. However, in 26.4 per cent of the cases in which vagotomy alone was performed without associated or previously performed procedures, motility was decreased or absent one to four years after operation. This was true in only 3.6 per cent of cases in which drainage operations had been combined with vagotomy or had been performed previously. Although reduction of gastric acidity continues in the majority of cases in the one to four year period, there is a tendency for gastric acidity to return, particularly when vagotomy alone has been performed. For example, in the immediate postoperative period, no change from preoperative levels was found in 6.5 per cent of the cases in which vagotomy without previous or simultaneously performed procedures was performed and in 8.0 per cent of cases in which vagotomy was combined with various drainage operations. However, in the one to four year period acidity returned to preoperative levels in 23.7 per cent of cases in which vagotomy was performed alone as contrasted with 7.0 per cent of cases in which associated drainage operations were performed previous to the vagotomy or simultaneously. Thus associated simultaneous or previous drainage operations definitely affect the long term effects of vagotomy on motility and acidity.

Whether it is necessary to sever all branches of the vagi is a difficult question to answer. Gregory and Ivy [10] said that it cannot be done in experimental animals. In 8 per cent of Bradley, Small, Wilson and Walters' [11] postmortem dissections of vagus nerves in 110 cases there were many branches, and division of all of them would be difficult. Moreover, in spite of the experience gained from a large number of gastric vagus resections there are at least 10 per cent and possibly as high as 20 per cent of the patients who, subsequent to operation, will be found to have positive reactions to the insulin test. At present, this is thought to be a test of the completeness of the vagotomy, but we believe that it is subject to question. Moreover, recurring ulcers and changes in motility with reductions of gastric acidity have occurred in patients with negative reactions to insulin tests as well as in those with positive reactions. In addition, as we have shown previously, there is a poor

11. Bradley, W. F.; Small, J. T.; Wilson, J. W., and Walters, W.: Anatomic Considerations of Gastric Neurectomy, J. A. M. A. **133**:459-461 (Feb. 15) 1947.

correlation of insulin reactions with unfavorable clinical results. From these results it seems that either all branches of the vagus need not be cut to accomplish all or part of the desirable results, or unfortunately in some cases the undesirable ones, or that a negative insulin reaction is not always indicative of a complete gastric vagotomy. However, generally speaking, when results of the test were considered negative by our criteria, a good correlation between the results of the test and the clinical results was obtained in 80 per cent of the cases.

Lastly, and of extreme importance, is a consideration of what happens to the peptic ulcer after vagotomy. Immediate relief of pain occurs. This probably is due to the dilatation of the stomach and the fact that gastrospasm cannot occur, for we know that the latter will cause the so-called ulcer type of pain. The relief of pain also may be due to a reduction of gastric acidity; this, however, does not always occur. Obviously, therefore, relief of the ulcer type of pain does not mean that healing of the ulcer has occurred. This was proved in a case in which roentgenologic and gastroscopic examination performed two years after operation revealed the same small gastric ulcer with associated gastritis that existed prior to vagotomy. Yet the patient was completely relieved of his symptoms of ulcer and had gained 20 to 30 pounds (9.1 to 13.6 Kg.). In another case spontaneous perforation of a duodenal ulcer occurred without evidence of such a perforation. It was found at postmortem examination 14 days after vagotomy and gastroenterostomy, together with a subdiaphragmatic abscess.

It is almost impossible to visualize duodenal ulcers of the first portion of the duodenum on gastroscopic examination or to determine the presence or absence of an active duodenal ulcer or of a gastrojejunal ulcer by roentgenologic examination unless a crater is seen. For these reasons such examinations are not of too great value in revealing the presence or absence of an ulcer except in the rare instances in which a crater can be demonstrated. The gastroscopic examination may be helpful in revealing the presence of an active gastrojejunal ulcer, but failure to reveal one does not mean that one is not there. The same errors occur in many cases in which vagotomy has not been performed. The point is that in general the diagnosis of recurring ulcer after gastroenterostomy or gastric resection is made on clinical symptoms, that is, a return of ulcer type of pain, and especially if melena, hematemesis or other symptoms or complications are present, regardless of the inability of the roentgenologic examination to demonstrate an ulcer. Thus, what criteria have we for determining whether a gastrojejunal ulcer has healed if the patient is denied the opportunity of determining the presence of a returning ulcer on the basis of pain as a result of the vagotomy? One of our patients was free of symptoms of ulcer for many months after gastric resection and later transthoracic vagotomy and therefore might have been thought to have had a healed gastrojejunal ulcer, but a severe silent hemorrhage occurred, and the roentgenologic examination revealed the crater of a gastrojejunal ulcer. Another resection of the stomach, with removal of the ulcer and subdiaphragmatic vagotomy, was performed. Insulin tests gave positive results both preoperatively and postoperatively. Tests of acidity before operation showed 12 units of free hydrochloric acid and after operation no free hydrochloric acid.

It is obvious, therefore, that it is difficult to estimate the number of patients who have had gastrojejunal ulcers which have healed after vagotomy. A similar situation exists among the patients who have undergone gastroenterostomy or gastric resection for duodenal ulcers along with simultaneous vagotomy.

We believe that the criteria for evaluation of clinical results of vagotomy performed alone and in combination with gastroenterostomy, pyloroplasty and gastric resection must be strict and that patients with symptoms of persistent disturbances of motility must be included in such evaluation and must be considered to have unsatisfactory results, since they certainly are not well. In our opinion, too, only patients with recurrence of ulcer proved by examination and laboratory studies should be included in the poor category since we have found that in some cases, as previously mentioned, recurrent ulceration was proved by examination in patients who had no ulcer symptoms, and several patients reporting symptoms of ulcer by letter or questionnaire had no evidence of recurrent ulceration on examination. In studying the methods of evaluation in every category, we have found that the results for patients reporting by questionnaire tend to be better than results in those who returned for examination. For example, 37 patients who underwent gastroenterostomy combined with vagotomy for duodenal ulcer replied by questionnaire: 89.2 per cent reported excellent results and 10.8 per cent unsatisfactory results. Only two of these patients reported symptoms suggestive of ulcer. These may be contrasted with 44 patients returning for examination, 75 per cent of whom had excellent results, 13.6 per cent unsatisfactory results and 11.4 per cent poor results. Statistically, insufficient numbers of cases in the other categories obviate their being mentioned. Therefore, when a large proportion of the evaluations are made by questionnaire only, we believe that the results will not only be inaccurate but will also appear too optimistic.

Another source of error in evaluating results arises from different criteria in the selection of patients for surgical treatment. At the Mayo Clinic all patients with ulcers are carefully screened by the medical department, and only those who have complications of duodenal ulcers, such as intractable pain, obstruction and hemorrhage (14 per cent of patients with duodenal ulcer), come to operation. Of course, if patients who have uncomplicated ulcer were subjected to operation, the results as measured by subjective relief of ulcer pain would be much better. On the other hand, we have found that from 60 to 70 per cent of patients with gastric ulcers who consult us should be operated on and gastric resection, with removal of the ulcer, performed.

We believe that differences in the criteria for evaluation of the results and for the selection of patients for operation are the main factors in explaining the great differences in the results obtained with gastric vagotomy by various surgical investigators throughout the country.

The experience of one of us (Walters) over a 30 year period is that a properly functioning gastroenterostomy will always heal a duodenal ulcer, reactivation of the ulcer occurring only with the development of a gastrojejunal ulcer which produces abnormal function of the gastroenteric stoma, usually with obstruction. Moreover, at the Mayo Clinic in the last 40 years, gastroenterostomy

alone for duodenal ulcer has yielded excellent results in approximately 85 to 90 per cent of carefully selected cases, and in only from 4 to 5 per cent [12] has proved gastrojejunal ulcer developed. The incidence of gastrojejunal ulceration after gastroenterostomy combined with vagotomy is paradoxically 11.4 per cent (five of 44 patients returning for examination). Thus in the small group of cases, vagotomy seems to have added nothing to gastroenterostomy in the prevention of gastrojejunal ulcer.

What is the objection to performing vagotomy routinely in cases in which posterior gastroenterostomy has been performed? The answer to this is that the disturbances of motility in the period following operations have been distressing to some patients and have prolonged the stay in the hospital to an average of 29 days. This should be contrasted with the average stay of 12 days after gastroenterostomy or resection without vagotomy. Some of these patients have loss of gastric secretion and electrolytes because the gastric retention requires gastric aspiration. In addition, they require almost constant attention, with frequently repeated determinations of chemical constituents of the blood and parenteral substitution therapy in order to maintain the fluid and electrolyte balance. This is not only discouraging to the patients but is also expensive, because of the many laboratory procedures necessary, the cost of the intravenous administration of fluid and electrolytes and the time required to treat the patient by the residents and the nursing staff. Even after the recovery of sufficient gastric motility for the stomach to empty or nearly empty, 13.6 per cent of patients have had side reactions, such as belching of foul gas, epigastric fulness or diarrhea, which have continued for many months.

The results of a properly performed adequate partial gastrectomy for duodenal, gastric or gastrojejunal ulcer are well known. Little detailed postoperative care is required, the results of the operation performed when indicated are excellent and the incidence of recurring ulcer after operations for duodenal ulcer does not exceed 2 to 2.5 per cent and is almost nil after operations for gastric ulcer. Whether an associated vagotomy will prevent the recurrence of ulceration in the 2 per cent of cases of duodenal ulcer remains to be seen. In our 331 cases there were 16 proved cases of recurring ulceration after vagotomy alone or associated with previously performed or simultaneous operations on the stomach. In addition, there were 12 cases of suspected recurrence of ulcer.

The final question which needs an answer is the one of what we consider to be the indication for vagotomy. The answer can be stated briefly as follows: We have been using the operation in the treatment of patients who have recurring ulceration after adequate partial gastrectomy. One of us (Walters) prefers to use the abdominal approach for this operation. Vagal resection, when the abdominal approach is used, can be as accurate as that carried out through the transthoracic method, and also the gastrojejunal anastomosis can be examined, the type of lesion present can be noted (for sometimes there is neither ulceration nor jejunitis) and the question of whether an adequate partial gastrectomy has previously been done (the roentgenologic determination of the percentage of stomach resected is fre-

12. Gray, H. K., and Williams, R. R., Jr.: Results of Classic Operations for Duodenal Ulcer: 5 to 10 Year Follow-Up in 532 Cases, J. A. M. A. **141**:509-512 (Oct. 22) 1949.

quently inaccurate) can be determined. In a few cases in which about two thirds of the stomach has not been removed an additional resection of the stomach has been performed with simultaneous vagotomy. The abdominal approach also permits exploration to determine whether other unsuspected lesions are present, such as gallstones, appendicitis or pancreatitis.

On our service we have used gastroenterostomy instead of partial gastrectomy in the treatment of certain large perforating duodenal ulcers, especially when removal of the ulcer, or allowing it to remain if in a low position and large, would not seem to permit a safe closure of the duodenal stump if partial gastrectomy or a partial duodenectomy were performed.[13] Resection of the vagus nerve is sometimes combined with gastroenterostomy for middle-aged, highly nervous persons with high levels of gastric acidity. Partial gastrectomy is the procedure that we prefer in the treatment of gastrojejunal ulcer after gastroenterostomy, the reason being that in our experience the risk of the operation is low and the results are excellent. For example, 53 patients had gastric resection for gastrojejunal ulcer at the Mayo Clinic in 1949, with a hospital mortality rate of 1.9 per cent. That this rate was not due to chance is shown by the fact that in 1948 the hospital mortality rate for 36 patients undergoing gastric resections for gastrojejunal ulcer was 2.8 per cent. The results of gastric resection for gastrojejunal ulcer have been reported by Priestley and Gibson[14] to be satisfactory in 87.4 per cent of cases. However, we believe that in certain cases of small gastrojejunal ulcers associated with bleeding and with gastrojejunitis after gastroenterostomy in which the function of the gastroenterostomy stoma is not interfered with (obstructed) as a result of the ulcer or its healing and in which the risk of gastric resection is increased, vagotomy alone is a worth while procedure.

Finally, it might be interesting to note that in 1949 surgical treatment was carried out for duodenal ulcer at the Mayo Clinic in 464 cases[15] (14 per cent of the cases in which a diagnosis of duodenal ulcer was made). Gastric resections were performed in 357 cases (77.0 per cent), with a hospital mortality rate of 1.1 per cent. Vagotomy alone was performed in 2 cases, gastroenterostomy and vagotomy in 40, gastroduodenostomy and vagotomy in 1, gastroenterostomy alone in 52 and other operations in 12. These statistics are like those for 1948,[16] when surgical treatment was performed in 429 cases of duodenal ulcer; 331 patients (77.1 per cent) underwent gastric resections (six with vagotomy), with a hospital mortality rate of 0.9 per cent. Three patients underwent vagotomy alone, 36 gastroenterostomy and vagotomy and 42 gastroenterostomy alone.

13. An exclusion type of operation even coning out the mucous membrane of the stomach but leaving the remaining layers of the pyloric segment is not considered an adequate operation for duodenal ulcer by one of us (Walters).

14. Priestley, J. T., and Gibson, R. H.: Gastrojejunal Ulcer: Clinical Features and Late Results, Arch. Surg. **56**:625-637 (May) 1948.

15. Walters, W.; Gray, H. K.; Priestley, J. T., and Waugh, J. M.: Report on Surgery of the Stomach and Duodenum for 1949, Proc. Staff Meet., Mayo Clin. **25**:571-581 (Sept. 27) 1950.

16. Walters, W.; Gray, H. K.; Priestley, J. T., and Waugh, J. M.: Condensed Report of Surgery of Stomach and Duodenum for 1948, Proc. Staff Meet., Mayo Clin. **25**:136-143 (March 15) 1950.

SUMMARY

A study of the physiologic and clinical results of vagotomy performed alone and in combination with gastroenterostomy, pyloroplasty and gastric resection has been made in three series of patients, series 1 representing 141 patients from one of the surgical services at the Mayo Clinic and series 2 representing 190 from the combined remaining surgical services at the clinic. The clinical results in both series are contrasted with those in series 3, a recent report of 2,558 cases collected by the Vagotomy Committee of the American Gastroenterological Association.

In the immediate postoperative period in cases in which vagotomy was performed alone without drainage operations such as gastroenterostomy and gastric resection, gastric free hydrochloric acidity has been reduced in 93.5 per cent of cases and to an achlorhydric level in 38.7 per cent. The acidity returned to preoperative levels in 23.7 per cent of cases over a period of one to four years. In only 7.0 per cent of the cases in which gastroenterostomy or resection was performed previously or in which either of these operations was performed at the time of vagotomy did acidity return to preoperative levels.

Gastric motility after vagotomy in the immediate postoperative period is likewise influenced by associated simultaneous or previously performed procedures, being absent or decreased in a greater percentage of cases when vagotomy was the only surgical procedure (72.9 per cent) than when associated pyloroplasty, gastroenterostomy or gastric resection was done (47.8 per cent). In the one to four year follow-up examination, motility continued to be absent or decreased in 26.4 per cent of cases in which vagotomy was the only procedure performed whereas it was absent or decreased in only 3.6 per cent in cases in which associated operations were done.

Our interpretation of the Hollander insulin test indicates that negative results were obtained in approximately 60 per cent of the cases in the immediate postoperative period and that this figure held well during later follow-up studies. Although there is a lack of correlation between the test and the resulting effects of vagotomy in some cases, generally speaking there was good correlation in 80 per cent of cases. However, in seven cases only one (posterior) vagus nerve was resected; vagotomy was performed in association with gastroenterostomy in six cases and with gastric resection in one case. Insulin tests gave negative results in four cases, and the test was unsatisfactory in one case and unfortunately was not done in two. In all cases there was marked reduction of gastric acidity from the preoperative level.

After treatment of duodenal ulcer with vagotomy alone 29 patients were followed one to four years in series 1 and 2. Excellent results were obtained in 62.1 per cent, unsatisfactory results in 31.0 per cent and poor results in 6.9 per cent.

When vagotomy was combined with gastroenterostomy for duodenal ulcer, results in 81 patients followed one to four years in series 1 and 2 were as follows: excellent in 81.4 per cent, unsatisfactory in 12.4 per cent and poor in 6.2 per cent. The poor results were based on surgical or roentgenologic evidence of proved gastrojejunal ulcer in all five cases. There is little evidence in our small series to indicate that vagotomy adds anything to gastroenterostomy in the prevention of gastrojejunal ulcer although it does produce lowering of gastric acidity in almost

all cases, and to an achlorhydric level in some. In fact, in some patients troublesome postoperative retention has prolonged hospitalization, increased the expense of maintaining the fluid and electrolytic balance and made necessary excessive and constant care by resident surgeons and attending nurses.

Vagotomy combined with pyloroplasty in nine cases of duodenal ulcer in series 1 and 2 followed one to four years showed excellent results in 55.5 per cent and unsatisfactory results in 44.5 per cent. There were no known recurrences of ulcers in this group.

Vagotomy and gastric resection in nine cases of duodenal ulcer in series 1 and 2 followed one to four years gave excellent results in 55.5 per cent and unsatisfactory results in 44.5 per cent. There were no suspected or proved recurrences of ulcer in this group. However, because of the associated postoperative vagal symptoms, it is felt that vagotomy probably was a detriment to gastric resection alone.

In the treatment of gastric ulceration, vagotomy alone was performed in 11 cases in series 1 and 2, which were followed one to four years, with excellent results in three (27.2 per cent), unsatisfactory results in five and proved recurrent ulceration in three (27.2 per cent). In three of the five with unsatisfactory results there was evidence of recurrent gastritis on gastroscopy. In two cases in series 1 vagotomy was combined with gastroenterostomy and excision of the gastric ulcer, with excellent results in both over one year periods.

In the treatment of gastrojejunal ulceration following gastroenterostomy, vagotomy alone was performed in 20 cases in series 1 and 2, and follow-up data are available for a one to four year period. Excellent results were obtained in 70 per cent, unsatisfactory results in 25 per cent and poor results in 5 per cent, with suspected or proved recurrent ulceration in the last group.

Of the five patients in series 1 and 2 followed one to four years in whom the gastrojejunal ulcer was excised, the openings in the stomach and jejunum closed, gastroduodenal continuity reestablished and vagotomy added, three (60 per cent) had excellent results and two (40 per cent) poor results with reactivation of the duodenal ulcer.

In the treatment of gastrojejunal ulceration following gastric resection, vagotomy alone was performed in series 1 and 2 in 29 cases. These were followed one to four years, with excellent results in 65.6 per cent, unsatisfactory results in 24.2 per cent and poor results in 10.2 per cent.

In three cases in series 1 in which a second resection of the stomach was combined with vagotomy, results were excellent in two cases on the basis of a questionnaire and unsatisfactory in one case 18 months, two years and three years, respectively, after operation.

In our opinion vagotomy alone for gastrojejunal ulceration after adequate gastric resection is a valuable addition to the armamentarium of surgical approaches for peptic ulceration when a difficult situation presents itself. With this procedure, 81.2 per cent of patients have been relieved of further symptoms of ulcer, the other 18.8 per cent having proved recurrence.

Further gastric resection and vagotomy may be another valuable procedure with good end results when gastrojejunal ulcer is found after inadequate gastric resection.

We believe that there is little place for vagotomy alone in the treatment of duodenal ulcer. In our opinion, vagotomy is indicated for duodenal ulcer only in the following circumstances. 1. It may be combined with gastroenterostomy in the treatment of certain highly nervous middle-aged men who have ulcers which are too large for safe removal and yet cannot be allowed to remain and thus prevent a safe closure of the duodenal stump if gastric resection is carried out. 2. It may be combined with pyloroplasty or gastroduodenostomy when the duodenal ulcer is small. For selected persons of the high tension type with large amounts of free hydrochloric acid, vagotomy may be combined with gastric resection.

Vagotomy should be reserved for poor risk patients with gastrojejunal ulceration after gastroenterostomy in cases of small ulcers or of gastrojejunitis, since much better results are obtained by undoing the gastroenteric anastomosis and the gastric resection. Disconnection of the gastroenteric anastomosis and reestablishment of gastroduodenal continuity combined with vagotomy are followed by a high incidence of reactivation of duodenal ulcer.

Vagotomy should not be performed for gastric ulceration because of the high incidence of an unsuspected malignant process and because postoperative persisting ulceration and gastritis and disturbances of motility make the results compare unfavorably with the excellent results obtained with gastric resection for this condition.

PRINCIPLES, PROBLEMS, PRACTICES OF ANESTHESIA FOR THORACIC SURGERY

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SEPARATION of essential procedures from the nonessential is one of the primary goals of the work done by my colleagues and me on anesthesia for thoracic surgery. We have tried and are trying to give answers to various problems in this field in terms of objective data. It seems to us that such a simplifying approach is necessary if procedures are to be soundly accepted or rejected. Clarification is important not only for the thoracic surgeon but for the well trained general surgeon who, more and more, is occupied with surgery in or through the thorax.

THE LOBECTOMY—PNEUMONECTOMY GROUP

In some clinics anesthesia procedures for lobectomy or pneumonectomy have varied considerably in recent years and have been growing more complicated. This contrasts with our practice, which has tended to become more stable and simple with the passage of time. The technic which has crystallized from the uncertainties of earlier years has developed gradually; the principles which serve as the basis for this technic will be emphasized in the following discussion.

During lobectomy or pneumonectomy one encounters most of the problems of anesthesia for all intrathoracic surgery. Special problems will be dealt with in separate sections, for example, thoracoplasty, transthoracic esophagectomy, thymectomy, surgery of the heart and the great vessels and problems arising in infants and small children. Except where otherwise specified, the procedures referred to are for adults of normal size.

MAJOR HAZARDS TO OVERCOME

The plan of anesthesia must be designed to overcome five somewhat overlapping major hazards: obstructing secretions, troublesome reflexes including cough, anoxia, abnormal elevation of the carbon dioxide tension of the blood, and circulatory strain.

OBSTRUCTING SECRETIONS.—*General Considerations:* Secretions found in the airway may be mucoid and nonirritating, or they may be composed of breakdown products of necrotic tissue highly irritating or infectious to the mucosa of the tract. (Acid gastric juice not infrequently is present in the pharynx and mouth.) They are potentially dangerous for two reasons: first, they may obstruct the airway and interfere with normal oxygen supply and carbon dioxide removal; second, when they are sprayed over the mucosa of the airway their irritant qualities may lead to pneumonitis or specific infections. The efficient evacuation of these secretions is therefore of importance before, during and after anesthesia.

Therapy: These secretions can be controlled and the danger from them minimized by antibiotics and by the following procedures.

Postural Drainage: Operation is not advisable in the early morning when large quantities of sputum have been present. Late morning or early afternoon is the optimum time for surgery in such instances. This allows time for elimination of secretions which may have accumulated during the night. Two hours before the operation is scheduled the patient should be placed for 15 to 20 minutes in a position which daily experience has shown to be most advantageous for drainage; he should be encouraged to raise as much sputum as he can. It is undesirable to delay this procedure to a time nearer the operation, for if that is done much of the sedative

From the Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital.

effect of the preanesthetic medication will be lost. Furthermore, if the drainage immediately precedes the induction of anesthesia, the irritation set up by the bout of coughing may not have subsided and the induction of anesthesia will be difficult by reason of the continued coughing.

In effect, the postural drainage is continued throughout the period of the operation, since for this and other important reasons (see below) the patient's head is lowered and maintained at about 20 degrees below the horizontal. In patients with much sputum it is not uncommon for several ounces of blood-stained pus to drain around the endotracheal tube into the face mask during operation. This must be aspirated before the patient is turned on his back at the end of operation.

Aspiration: When postural drainage is not adequate, it may be necessary in rare cases to subject the patient to bronchoscopy and then aspirate any obstructing material shortly before the induction of general anesthesia. (The pros and cons of bronchoscopy at the end of operation are considered later.)

As soon as possible after the induction of anesthesia an endotracheal tube is introduced. Aspiration should be carried out almost at once after this tube is in place when the patient has had a history of considerable sputum or if sounds of sputum in the airway are present. Again, aspiration will be indicated when the pleura is opened, for then secretions will be expressed into the main bronchi as the diseased lung collapses. These secretions may gush into the main air channels and require swift, efficient removal, possible only if an endotracheal tube is in place and an aspirating catheter at hand. It is important to have the respiratory system open when aspiration is being carried out, otherwise total deflation of the lungs may occur.

The flow of secretions into the airway may be particularly troublesome whenever the surgeon elevates or mobilizes the lobe. Auscultation of the lungs should be frequently carried out by placing one of the breathing tubes of the anesthesia machine at the anesthetist's ear. The possibility of a sudden profuse hemorrhage from a disease cavity or tumor must always be considered. If this happens, rapid aspiration offers the only hope of saving the patient until the surgeon can get a tourniquet around the diseased lobe. Whenever the tourniquet is released as a step in the operative procedure, the anesthetist must be alert to the possibility of endobronchial hemorrhage. This danger is ever present.

Occasionally patients undergoing a thoracic operation are said to drown in their own secretions. With an endotracheal tube and bronchial aspiration this should not happen. When secretions are overwhelming or when the airway becomes blocked by fragments of tissue or blood clots, bronchoscopy may be of lifesaving importance in certain desperate cases. Its routine use is neither necessary nor desirable. The reasons for this will be discussed later.

Medication: The formation of saliva and mucus should be minimized with the use of atropine.

Troublesome Vagal Reflexes of the Respiratory and Circulatory Systems.—*Cough.*—Cough normally depends on local irritation in the air passages. It can be initiated elsewhere by irritation of afferent vagal fibers. In either case impulses are transmitted by afferent vagal fibers. The reflex arc is completed by motor nerves which carry efferent impulses to the intrinsic and accessory muscles of respiration. In addition to these factors an efficient cough requires not only

closure of the glottis but also a closed chest wall, in order that pressure in the airway may be built up by action of the muscles involved in forced expiration.

The action of cough on material in the tracheobronchial tract was considered by Ameuille.[1] He introduced iodized oil into a lung with cavitation in the right lower lobe and observed with successive coughs that the foreign material was transferred by stages from the cavity, first to the middle lobe, and then to the contralateral lower lobe, and finally was expelled. These observations demonstrated that while cough partially clears the airway of irritant material it also first spreads that material widely in the lungs.

This subject was later studied in more detail by Brown and Archibald.[2] They have called attention to several points which are important in the present consideration: While any foreign substance in the tracheobronchial tree may stimulate cough, tolerance to the excitation is rapidly obtained. The excitability of various parts of the pulmonary tree varies widely, from extreme irritability in the trachea and large bronchi to practically none in the small bronchi. These authors point out that while cough certainly has as its function the clearing of the airway, it may have the opposite effect. It is usually preceded or followed by a quick, rather deep inspiration which may move foreign material deeper into the airway, into the insensitive peripheral regions where it cannot initiate further cough reflexes.

During surgical intervention within the chest, cough cannot be successful for, as pointed out, one of the requisites of an efficient cough is the development of a relatively high pressure in the airway. Plainly this cannot be accomplished when the chest is open. Straining in the attempt to cough will cause a sudden ballooning of the lung on the side of the open pleura and spread of pus into the normal lobes of that side. The position of the patient during intrathoracic surgical procedures restricts the efficiency of cough. Since cough has an objectionable spreading action as well as a beneficial expulsive effect, it is undesirable during operation, when the airway may contain infectious or irritating material, as it repeatedly does during operations on a diseased lung. Cough is also dangerous during intrathoracic procedures because of the technical difficulties and hazards which it imposes on the surgeon. An endotracheal tube prevents closure of the glottis and the building up and sudden release of endobronchial pressure; in this way, by preventing cough, it helps to prevent the spread of material. It is a mistake, we believe, to preserve the cough reflex during the type of surgery under discussion. It is better to provide conditions in which the cough reflex will not be active and to remove undesirable material from the air passages by aspiration. The anesthetist, and not the patient, should assume the responsibility of maintaining free air passages during and immediately after the operation.

Other Vagal Reflexes.—Patients vary widely in their response to mechanical stimulation of branches of the vagi. Occasionally surgical intervention in the lung, particularly when the pleura is inflamed or when the operation involves the region of the hilus, will cause extreme variations in respiratory rate and force. Apnea

1. Ameuille, P.: Injection transpariétale de lipiodol dans une caverne pulmonaire: Production sous l'écran du phénomene de l'emboli bronchique, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:791-793, 1924.

2. Brown, A. L., and Archibald, E.: The Action of Cough upon Material in the Tracheo-Bronchial Tract: Experimental Study, Am. Rev. Tuberc. **16**:111-122, 1927.

punctuated by abrupt, irregular, forceful inspirations may occur. This makes operations in the region difficult and dangerous. At times stimuli around the hilus cause great slowing of the pulse rate. These reflexes may make for inefficiency of the heart's action. Cases of cardiac standstill have been attributed to a vagal reflex. This catastrophe has not been observed by us.

Therapy.—The dangers introduced by certain vagal reflexes have been described above. These reflexes can be depressed, if not eliminated, by the following procedures.

Preanesthetic Medication: Atropine frees the vagus to a considerable extent from the effects of stimulation. Accordingly, relatively large doses are useful in minimizing these reflexes.

General Anesthesia: It is not possible to eliminate these reflexes by safe levels of general anesthesia. It is possible, however, to diminish their effects by deepening the anesthesia when the surgeon is operating around the hilus or when he places a tourniquet around a lobe. There is some reason to believe that ether is more effective for this purpose than are the other general anesthetic agents used in thoracic surgery.

Local Anesthesia: In cases in which vagal reflexes prove troublesome, a useful procedure is to inject 1 per cent procaine directly into the main trunk of the vagus in the upper mediastinum between the recurrent nerve and branches to the pulmonary plexus. This block can be reenforced by injecting 15 or 20 cc. of 1 per cent procaine under the parietal pleura over a circular area surrounding the hilus, about 10 cm. in diameter.

ANOXIA.—The normal oxygenation of the body during anesthesia and thoracic operations is handicapped by several factors.

Obstruction of the Airway.—This can occur from new growths, but more often it occurs as a result of draining secretions or blood. These have already been discussed.

The Open Pleura.—This interferes with proper oxygenation of the body not only because it allows the intrapleural pressure to reach the atmospheric level and thereby restricts pulmonary ventilation but also because it allows swinging of the mediastinum with each respiratory effort unless it is unusually rigid or has been fixed as a result of previous inflammation and scar tissue formation. The mediastinal swing limits the ventilation of the contralateral lung and also increases the technical difficulties of thoracic surgery, but, perhaps equally important, it gives rise to reflexes which result in a fall in blood pressure. The open pleura interferes, therefore, not only with the intake of oxygen but also, by crippling the circulation, with the distribution of oxygen in the body.

Therapy.—Anoxia must be avoided. To this end an anesthetic agent is used which permits the use of a high oxygen percentage (about 95 volumes per cent with ether). The following procedures are important factors in avoiding an oxygen deficit.

Factors Already Considered Which Are Applicable Here: The use of atropine diminishes the reflexes which cripple the respiration and circulation. It reduces the quantity of mucus and saliva formed. The use of an endotracheal tube and

aspiration of secretions are important. The endotracheal tube facilitates efficient artificial respiration when needed. In some cases bronchoscopy may be indispensible.

Positive Pressure Anesthesia: This requires general anesthesia and a closed anesthesia system. The apparatus for this can be of various types as long as it includes (*a*) a breathing bag, (*b*) a soda lime filter for removing excess carbon dioxide, (*c*) oxygen and (*d*) the anesthetic agents. To be dependable in all cases positive pressure anesthesia requires a free airway; this can be ensured only if an endotracheal tube is in place. (In lobectomy for chronic lung abscess previously drained by thoracotomy the situation is frequently complicated by the presence of a bronchocutaneous fistula. If this is large, much time will be saved as well as the hazards of an unduly prolonged induction avoided if the fistula is closed by means of a sterile gauze pack stoutly reenforced and held in place with adhesive tape.) Positive pressure should be introduced over a period of several seconds and all sudden overdistention of the lungs avoided. From the physiological standpoint, probably an even longer period is desirable. The correct degree of distention should be arrived at by discussion between the surgeon and the anesthetist. Practically, if one must combat untoward reactions in the patient, the changes must be fairly rapid. Occasionally abrupt changes in positive pressure may be unavoidable as when a sudden gush of pus or blood into the bronchi requires immediate aspiration. The patient will usually tolerate a few abrupt changes in pressure, though occasionally these may produce severe circulatory reaction, shown by low blood pressure and poor color, and are to be avoided when possible.

The surgeon can frequently work more swiftly and efficiently in the presence of a collapsed lung; therefore the use of positive pressure should be delayed until one of the following indications for it appears. The appearance of cyanosis is a sharp warning of the necessity of using positive pressure provided other causes of the cyanosis, such as an obstructed airway, have been eliminated. In secondary operations and in cases of extensive and prolonged sepsis, the mediastinum will usually be fixed by scar tissue. If this is not the case, the mediastinum swings back and forth with respiration. Positive pressure anesthesia is indicated here and checks the condition. In long and difficult operations in the open chest the pulse rate may rise; occasionally the blood pressure increases gradually, or it may fall. These abnormalities when due to anoxia can frequently be overcome by the use of positive pressure, even though the other indications have not been present.

Periodic reexpansion of collapsed lobes during a prolonged operation is advisable. No lobe should remain collapsed for more than 20 minutes at a time, often less. Inflation will help to demonstrate pathologic changes characterized by atelectasis. It is unwise to attempt to reexpand lung segments collapsed for a long time by disease, for such a procedure has been seen to result in pulmonary edema. This has developed directly under observation in the involved area. Periodic reexpansion is useful in demarcating areas to be excised in segmental pulmonary resection.

Positive pressure should be used to inflate the remaining lobes at the end of operation. This inflation must be artificially maintained until the chest is tightly closed; then the pressure in the airway may be gradually diminished. Positive pressure can be regulated through the cooperation of the surgeon and the anes-

thetist. Manometers serve no useful purpose and are likely to distract attention from more important matters. When inflation of the lung is to be carried out, the anesthetist slowly increases the pressure in the breathing bag until the surgeon indicates that an adequate degree of expansion of the lung has been attained. Occasionally the pressure in the breathing bag rises to what seems to the anesthetist to be the upper limit of safety and the lung has not yet expanded. In this case, the rise of pressure is checked and the cause for the unusual condition sought. Generally it is found to be due to secretions blocking the airway, to too rapid elevation of pressure or to an endotracheal tube which is too long and has entered the bronchus of the contralateral lung. The anesthetist should, of course, familiarize himself with the feel of various bag pressures by experience with a bag and manometer set. It is doubtful if the pulmonary pressure in an adult should ever exceed 20 cm. of water pressure, and in children less than this is used.

TABLE 1.—*Arterial Blood* *

		Before Operation			Time After Pleura Open (Min.)	At Operation's End		
Operation	No. of Patients*	O_2 Content, Volumes %	% Saturation	Hematocrit % Cells		O_2 Content, Volumes %	% Saturation	Hematocrit % Cells
Pneumonectomy	16	15.7	95	42	122	15.2	94	46
Lobectomy	20	16.7	96	43	96	16.3	97	45
Miscellaneous	7	17.5	95	46	58	17.5	97	46

				Alveolar CO_2					Alveolar CO_2	
Operation	No. of Patients	CO_2 Content, Volumes %	p_H	Tension, Mm. Hg.	Volumes %	Time After Pleura Open (Min.)	CO_2 Content, Volumes %	p_H	Tension, Mm. Hg.	Volumes %
Pneumonectomy	16	59.0	7.48	35.0	4.9	122	59.6	7.09	98.0	13.7
Lobectomy	20	57.4	7.51	32.8	4.6	95	57.9	7.22	66.6	9.3
Miscellaneous	7	58.1	7.52	32.2	4.5	58	57.4	7.37	44.0	6.2

* For details see Beecher, H. K., and Murphy, A. J.: Acidosis During Thoracic Surgery, J. Thoracic Surg. **19**: 50-70, 1950.

The relationship of positive pressure in the airway to circulatory strain is discussed later; so also is the use of intermittent positive pressure, "assisted respiration," in maintaining a normal carbon dioxide tension.

How well anoxia can be prevented or overcome is shown by the average data in table 1. Reference to the paper [3] from which the data come shows that anoxia has been prevented in almost all the individual cases used in making the averages.

ELEVATION OF THE ARTERIAL CARBON DIOXIDE TENSION.—The chain of events that leads to success or failure in thoracic surgery is more complex than it is in other fields. Notwithstanding the progress made in the last decade or two, an occasional patient succumbs near the end of operation or shortly thereafter or more often barely pulls out of a puzzling condition of low blood pressure. There is good reason to believe that some of these accidents are due to the accumulation of carbon dioxide even when the oxygenation of the patient is normal (table 1).

3. Beecher, H. K., and Murphy, A. J.: Acidosis During Thoracic Surgery, J. Thoracic Surg. **19**:50-70, 1950.

The principal data are summarized in table 1 in order to compare the patient's state near the end of operation with what it was at the beginning. The constancy of the carbon dioxide content shows the folly of neglecting p_H measurement when blood levels of this gas are considered. The important thing here is pressure of carbon dioxide. We have shown that the rise in alveolar carbon dioxide tension begins and develops to a significant degree before the pleura is opened.

The patients referred to in table 1 were all operated on under ether anesthesia. It is commonly stated that ether anesthesia is associated with a condition of clinical acidosis. This is incorrect, as shown elsewhere.[4] Ether anesthesia, even when long and deep and used in old persons, does not itself produce clinical acidosis and therefore was not responsible for the fall of p_H with the great rise of carbon dioxide tension encountered in thoracic surgery. The acidosis here is to be explained largely if not entirely by interference with pulmonary ventilation.

In the normal, unanesthetized person an increase in the concentration of carbon dioxide in the inspired air results in an increase in pulmonary ventilation, until about 9 per cent is reached. Further increase in carbon dioxide causes depression of the respiration,[5] presumably due to the well known anesthetic properties of the gas. During thoracic surgery, no such respiratory response to the high tensions of carbon dioxide has been evident, probably because of the depression of the respiratory centers.[6]

It is clear that in the circumstances being considered (unlike the normal) respiration adequate to provide oxygen is not adequate to remove carbon dioxide. Preoccupation with the color of a patient's blood, important as this is, is not enough. It is only half of the problem. The carbon dioxide level must also be considered. The tensions of this gas reached in some of our patients might of themselves be fatal, particularly in patients who had been subjected to considerable blood loss and to surgical trauma. Why the carbon dioxide tension should rise so high must be considered. This is not the usual effect of ether with patients in the supine position. Work in progress supports the view that this great rise is to be blamed on interference with the respiration caused by unfavorable position and the open pleura and that even without assisted respiration patients will excrete carbon dioxide adequately in most cases in the prone or supine positions. Depression of respiration by overdose of the anesthetic can be a factor. Some further facts to be scrutinized in this connection are the following.

In 11 patients the alveolar carbon dioxide tension was determined immediately prior to the induction of anesthesia and then some 42 minutes later but before the pleura was opened. (These patients had been in the operative position with the diseased side uppermost for approximately 20 minutes of this time.) Ten of these 11 patients showed a rise in alveolar carbon dioxide tension of 14.6 mm. of mercury, or 2.0 volumes per cent, on the average. Thus the alveolar carbon dioxide

4. Beecher, H. K.; Francis, L., and Anfinsen, C. B.: Metabolic Effects of Anesthesia in Man: I. Acid-Base Balance During Ether Anesthesia, J. Pharmacol. & Exper. Therap. **98**:38-44, 1949.

5. Pitts, R. F., in Howell, W. H.: Textbook of Physiology, edited by J. F. Fulton, and others, ed. 15, Philadelphia, W. B. Saunders Company, 1946, p. 914.

6. Dripps, R. D., and Dumke, P. R.: The Effect of Narcotics on the Balance Between Central and Chemoreceptor Control of Respiration, J. Pharmacol. & Exper. Therap. **77**:290-300, 1943.

tension had begun to swing up sharply before the pleura was opened and while the tidal volume and minute volume of respiration appeared to be normal. The open pleura is therefore not the only factor responsible for the later rise in carbon dioxide tension. It must be emphasized that this increase in alveolar tension of 14.6 mm. of mercury is a truly great rise. For example, in the normal unanesthetized person a rise of only 1.0 volume per cent in the alveolar carbon dioxide content is sufficient to increase the pulmonary ventilation about 50 liters per minute. It has been found [7] that a rise in pressure of 1.6 mm. of mercury will double pulmonary ventilation in the average person.

How can this early rise in alveolar tension of carbon dioxide be explained? A number of factors are present. Besides the position, we must consider the increase in dead space produced by the anesthesia apparatus, the effect of the endotracheal tube and possibly the effect of the anesthetic agent on the bronchiolar musculature. Conceivably an increase in dead space could be caused by the effect of the anesthetic (ether) on these muscles. If it leads to hypoventilation, overanesthetization can, of course, cause the carbon dioxide content to rise.

The statement is sometimes made that the answer to all these problems is mechanical respiration. There is perhaps still some room for doubt concerning this. For one thing, the mechanical respirators used with anesthetic agents have proved to have a mortality rate of their own due to explosion. The unsatisfactory ventilation sometimes produced by these machines is well known. It is widely accepted that respiration carefully assisted by the anesthetist's squeezing the bag just as the patient inspires gives an effective type of ventilation. In a study of this problem we have been able to keep the carbon dioxide tension at a normal level in only one third of the pneumonectomy cases by the most effective type of ventilation we can provide. Studies are now under way to compare the effects of various operating positions.

The serious effects of the carbon dioxide tensions achieved at the end of long operations through the thorax can be inferred from the abundant evidence on this score found in persons not under anesthesia. Possibly the anesthesia may afford some protection. It seems unwise to depend on that.

Goldstein and DuBois [8] have shown that a fall of blood pressure immediately follows the cessation of rebreathing of high concentrations of carbon dioxide. Dripps [9] has discussed the fall of blood pressure which occurs when the subject ceases to get cyclopropane. He reports that under this agent the carbon dioxide tension rises to great heights and that a considerable fall of blood pressure sometimes occurs when the administration of cyclopropane is terminated. ". . . the higher the tensions of this gas (carbon dioxide) in the arterial blood the greater is the likelihood of a postanesthetic decrease in blood pressure . . ." After the end of the surgical procedure and the change of the patient's position to a more favorable one, the p_H rises and the carbon dioxide tension is reduced. The stimulant

7. Campbell, J. M. H.; Douglas, C. G.; Haldane, J. S., and Hobson, F. G.: The Response of the Respiratory Center to Carbonic Acid, Oxygen, and Hydrogen Ion Concentration, J. Physiol. **46**:301-318, 1913.

8. Goldstein, J. D., and DuBois, E. L.: The Effect on the Circulation in Man of Rebreathing Different Concentrations of Carbon Dioxide, Am. J. Physiol. **81**:650-660, 1927.

9. Dripps, R. D.: The Immediate Decrease in Blood Pressure Seen at the Conclusion of Cyclopropane Anesthesia: "Cyclopropane Shock," Anesthesiology **8**:15-35, 1947.

action of the carbon dioxide is withdrawn, and the blood pressure falls. As pointed out above, there is reason to believe that this is a true cause and effect relationship. The relevance of these findings to the fall of blood pressure often found at the end of thoracic surgical procedures is unproved, of course, but a true relationship is probable.

Experience has shown that one can usually obtain what appear to be satisfactory results with patients in the position generally used (lung being operated on uppermost) and with only occasionally assisted respiration. The disturbing inference remains that the occasional bad results mentioned earlier may in some cases be directly related to the high carbon dioxide tensions reported here. Possibly surgeons working through the open thorax may decide that they prefer to accept the real hazards of the high carbon dioxide tensions mentioned, which arise as a consequence of common present practices. They may decide that intrathoracic operation on patients in the supine or prone position is more dangerous than increased carbon dioxide tensions. This is beyond our competence to discuss. However, reconsideration must be given to what constitutes the truly optimum position for operation, and more study based on data obtained in man must be given to effective means of assisting respiration during thoracic procedures.

Circulatory Strain.—*The Heart.*—The stress and strain of the procedures and even direct pressure by the surgeon on the heart in thoracic operations interfere with normal cardiac function. Anoxia quickly damages the heart, and it dilates rapidly. This has been observed clinically and in the laboratory many times. Unless such a cycle is broken at once the patient will die. Not only is the heart's action frequently irregular under cyclopropane but its action at times appears to be less vigorous under cyclopropane than under ether. This is discussed in the section on the choice of the anesthetic agent.

Pulse Rate.—In broad terms one can say that a pulse rate that swings up during anesthesia is ominous and a falling rate a good sign. The trend of the pulse rate has some importance, but absolute rates at any given time are often misleading guides as to the patient's condition. An unexplained rapid pulse rate will sometimes call attention to anoxia that might otherwise have been overlooked. Mechanical stimulation of the cardiac nerves, and even of the heart itself, produces confusing signs. The unreliability of the pulse rate in judging the condition of the circulation has been emphasized [10] by a study of 106 newly wounded men in which it was shown that the pulse rate is of no help in judging degree of shock. When one compares patients without shock with those having severe shock, it is apparent that the minimum, maximum and average pulse rates are not significantly different in the two groups.

Blood Pressure.—While pulse rate is often a misleading guide, pulse quality is a sign of great value for the anesthetist. A weakening pulse is always a sharp warning of impending danger. A weak pulse is usually associated with low blood pressure. Blood pressure can be adversely affected by careless and sometimes necessary use of positive pressure in the airway. At times patients will not tolerate without a fall of blood pressure even moderate increase in pressure in

10. Beecher, H. K.; Simeone, F. A.; Burnett, C. H.; Shapiro, S. L.; Sullivan, E. R., and Mallory, T. B.: The Internal State of the Severely Wounded Man on Entry to the Most Forward Hospital, Surgery **22**:672-711, 1947.

the airway; other patients show signs of a deteriorating circulation as the elevated pressure is maintained. Patients in good condition will tolerate a mean pressure of 10 cm. of water (above atmospheric pressure) for 20 or 30 minutes or more, but the circulation of patients in a precarious condition often will deteriorate rapidly. This has been demonstrated in the clinic many times. It was shown rather precisely in an experimental study [11] in dogs when the airway pressure was raised to 10 cm. of water (mean pressure) with spontaneous respiratory fluctuations in pressure oscillating about this figure. In these cases the duration of elevation was usually 10 ± 2 minutes. When the animals were in bad condition from hemorrhage or deep anesthesia, the pressure was released much sooner to avoid killing the subject.

Elevation of pressure in the airway in these experiments caused great elevation of central venous pressure, some fall in systolic, diastolic and mean arterial pressure, a narrowing pulse pressure and a decrease in flow in femoral and carotid arteries and in the superior mesenteric vein. There were no consistent significant changes in hydraulic impedance in the three vascular beds referred to and no consistent significant changes in heart rate. Release of pressure in the breathing bag tended to restore these factors to their original values, except in certain subjects in bad condition.

The probable reason for the difference in tolerance of subjects in good condition and of those in shock can be deduced from the pressure changes observed. The difference between mean central arterial and mean central venous pressure provides the motive force which drives the blood through the peripheral vessels. Elevated pressure in the airway causes a rise in venous pressure as well as a fall in arterial pressure; thus the adverse effect on the circulation is greater than if arterial pressure alone were affected. A comparison of actual pressure changes in a dog in good condition with similar changes in a dog in shock serves to illustrate this point and to bring out differences between them, which are masked by the mean figures in the article referred to.

In a typical instance, a dog in good condition before elevation of pressure had a mean arterial pressure of 133 mm. of mercury and a central venous pressure of 0.0 mm. of mercury, giving an effective perfusion pressure of 133 mm. After elevation of pressure in the airway, the arterial figure was lowered to 126 mm. and the venous raised to + 5.0 mm., yielding an effective perfusion pressure of 121 mm. Although the mean arterial pressure was lowered only 7 mm. by elevating pressure in the airway, the effective perfusion pressure was lowered by 12 mm. It is obvious that the perfusion pressure of 121 mm. of mercury after elevation is adequate to maintain a brisk peripheral flow, and the animal tolerated this elevation well.

In a corresponding typical instance in a dog in shock, mean arterial pressure before elevation was 44 mm. and central venous pressure — 2.7 mm. of mercury, giving an effective perfusion pressure of 46.7 mm. After elevation of pressure in the airway, the mean arterial pressure was 41 mm. and the mean venous pressure + 3.2 mm., giving an effective perfusion pressure of 37.8 mm. Thus, although the mean arterial pressure fell only 3 mm., or 7 per cent, the effective perfusion pressure fell 8.9 mm., or 19 per cent. In this typical instance, flow through the

11. Beecher, H. K.; Bennett, H. S., and Bassett, D. L.: Circulatory Effects of Increased Pressure in the Airway, Anesthesiology **4**:612-618, 1943.

peripheral vessels showed a marked decrease, the animal progressively declined and after ten minutes of elevated pressure in the airway, the mean arterial pressure had fallen to 29 mm. and the mean perfusion pressure to 24.7 mm., a 47 per cent fall from the preelevation pressure. Presumably, increased pressure in the airway interferes with the flow of blood through the lungs and impedes the emptying of the right side of the heart and the filling of the left, with consequent rises in central venous pressure. Judging by the consistency of the decreased flow in femoral, carotid and mesenteric veins, it seems safe to assume that cardiac output likewise falls. Finally, it should be observed that deep anesthesia magnified the seriousness of the effect of the increase of pressure in the airway.

These examples offer at least a partial explanation of why an elevation of pressure in the airway is of little moment in subjects in good condition, whereas in subjects with arterial pressure already critically low, as in shock, increased pressure in the airway may work harm far beyond that to be expected from the fall in arterial pressure alone. The observations on dogs provide a physiological explanation for the clinical observation that patients in shock do not tolerate well increased pressure in the airway. They indicate that this procedure is not innocuous and suggest that although it is perhaps relatively safe in patients in good condition it is dangerous and may be deadly in patients in shock or in otherwise poor condition. When it introduces additional stresses in a patient in poor condition he may be overwhelmed.

In clinical practice, 10 cm. of water is a moderate mean pressure. Higher pressures in the breathing bag are in common use, often for prolonged periods. The effects on the circulation of these higher pressures probably would be greater and in certain cases more deleterious than the effects of pressure of 10 cm. of water. (Pressure for expanding collapsed lung tissue in the presence of open pneumothorax probably should never exceed 20 cm. of water and this for only a few minutes.)

Reduced Circulating Blood Volume.—This may be indicated by low blood pressure, or it may be latent, masked by compensatory reactions of the body. The latter is more usual, before the end of the operation at least. A number of factors are responsible for the diminution in blood volume in these cases. Elective thoracic operations are often scheduled in the warm summer months and sweat loss is a factor. Pleural and mediastinal reflexes already described are important; prolonged surgical procedures and blood loss, overanesthetization and chilling or overheating of the patient lead to a low blood pressure and surgical shock, with the result that the oxygenation of vital structures is impaired.

Therapy.—Position [12]: Patients are operated on with the diseased side vertically uppermost and a blanket roll or pillow of approximately 5 inches (13 cm.) in diameter placed beneath the thorax. About 5 degrees of Trendelenburg position is used and then the operating table kept flat for some surgeons and broken 10 to 15 degrees at the head and 5 degrees at the foot for others. The possibility of cerebral air emboli is thus minimized, the position is more convenient for the surgeon, drainage from the airway around the endotracheal tube is promoted and if the circulating blood volume is seriously reduced the vital structures will get a better supply of blood in this position than in the horizontal one. Laboratory findings and also

12. See discussion of position in relationship to carbon dioxide retention.

long clinical use of the "shock position" for maintaining an adequate cerebral circulation offer abundant evidence of the value of this position in combating a low systemic blood pressure.

Restoration of the Circulating Blood Volume: Except in the most desperate emergencies intrathoracic operation is never undertaken until the concentration of hemoglobin in the blood has been restored to normal or nearly so. The patient receives blood transfusion during the surgical procedure whether impairment of the circulation is apparent or presumed to be latent. Five per cent glucose solution in distilled water is temporarily useful in restoring fluid loss. There is some evidence that the glucose spares liver glycogen during anesthesia and helps to maintain the patient in good condition. Considerable caution must be exercised in the intravenous administration of fluids, for their careless use may lead to overload of the circulatory system, which is already under a considerable strain, with resulting pulmonary edema.

Inspection of table 1 shows that even in the total pneumonectomy group, the oxygen saturation, near the end of operation remains almost normal in the average case. Indeed, it can be found by inspecting the data recorded in the paper from which this table was taken [3] that usually this holds for the individual case as well as for the average. However, there are occasional patients who must undergo pneumonectomy when the lungs have been impaired, as, for example, those with emphysema or silicosis, who may have persistent cyanosis. In such cases a recurrent discussion revolves around whether a blood transfusion will be more of a benefit than a hazard. Certainly in patients undergoing total pneumonectomy a real hazard can arise from overloading the circulating blood volume with infusions, whether of electrolytes or of whole blood. If these exceed in quantity what the body can adjust to, pulmonary edema results. This edema may be of serious degree. On the other hand, if blood replacement is not kept fairly near blood loss, disastrous fall of blood pressure may occur either during the operation or shortly thereafter.

One group argues, bearing in mind the hazard of pulmonary edema, that even though cyanosis is present, no important gain is to be derived from blood transfusion if the blood pressure is satisfactory. This group holds that the patient's blood is already far from saturated; although the hemoglobin is combining with all the oxygen it can get it is not being satisfactorily oxygenated in the active circulation. Therefore, they ask, what is to be gained by giving more hemoglobin (whole blood) which will only overload the circulation?

Another side of this complex problem must be considered. Even though all the blood passing through the lungs is not saturated, the degree of unsaturation of the mixed venous blood is a factor that must be taken into account. One could argue that the rate of circulation of blood in the peripheral tissues might have been slowed down when the circulating blood volume fell as a result of the blood loss during surgical intervention. Increase of blood volume by transfusion would increase the rate of circulation in the peripheral tissues, and therefore the degree of unsaturation of the mixed venous blood would be less and this in turn would reduce the job of oxygenation to be done in the lungs as the blood passed through. The result could well be reduction of the cyanosis (reduction of unsaturation). Another

problem hinges on whether the cells will get more oxygen when the saturation is reduced from 80 to 60 per cent, for example, than when it is reduced from 70 to 30 per cent.

If the patient receives inadequate transfusion for any reason, one must bear in mind that when he is moved at the end of operation he will usually have a fall of blood pressure because of the deficient circulating blood volume. Therefore, facilities should be ready so that blood can be forced into the veins by syringe through a three-way stopcock to avoid the dip in blood pressure. Persistent low blood pressure can sometimes best be overcome by intra-arterial transfusion of whole blood. (Fall of blood pressure at the end of the operation may be due to removal of the patient from a high carbon dioxide atmosphere. This has been discussed previously.)

There are many problems for which we need more data. When definite information is lacking, a middle course must be pursued between overloading the circulation and allowing too great a difference between blood loss and blood replacement to arise. Most of our patients, having started with a normal hemoglobin content, receive about 1,000 cc. of whole blood during an uncomplicated pneumonectomy. When unusual hemorrhage occurs, the amount is greatly increased. It must be anticipated that the plasma from at least 500 cc. of whole blood will pass into the pleural space postoperatively as a result of pleural trauma during surgical intervention.

EQUIPMENT AND ITS USE FOR ANESTHESIA IN THE LOBECTOMY-PNEUMONECTOMY GROUP

The reasons for most of our procedures have emerged in the preceding discussion of the hazards encountered and how they can be overcome. Therefore a brief description of the equipment used will be sufficient except for a few controversial matters.

Any factors which contribute to the safety and success of the operation are considered essential, and any not distinctly in this category are to be eliminated, even though not clearly bad. Many innovations in this field can be ruled out on logical grounds; others must be tried out. Here is the record of our attitude at the present time toward various practices recommended for use in anesthesia for thoracic surgery, with what we hope are logical reasons for or against the adoption of many of the practices discussed in this field and labeled indispensable at various clinics. Some continuity is given to an otherwise disjointed examination of current practices by their application or rejection in our technic.

With standardization of surgical procedure, it may be expected that more thoracic operations will be carried out by a greater number of surgeons. In some cases this may be desirable, yet as long as the anesthesia technic is pictured as possible only for an expert with wide experience and much equipment, it is not likely that even "standardized" thoracic operations will be attempted in any except the large clinics. Whether these operations should, even when standardized as much as possible, be turned over to the surgeon who performs occasional thoracic operations is not a question for me to attempt to answer. Certainly any such evolution cannot occur unless it can be shown that good anesthesia can be provided for these operations by the average well trained anesthetist, who may have wide experience in providing anesthesia for general surgery yet little experience in thoracic surgery.

Therefore, a further aim has been to see if we could develop a sound technic with the simple apparatus found in or easily obtainable by all hospitals. The test of our results must be that they equal or excel those obtained with more complicated technics and apparatus.

ANESTHESIA MACHINES.—General anesthesia with an oxygen-rich atmosphere induced through a closed system with a breathing bag and carbon dioxide absorber, usually of the "circle" type for adults and the "to-and-fro" type for children or cachectic adults (the latter has a tendency to get hot and may require changing several times in a single operation), facilities for the utilization of positive pressure in the airway as needed, for aspirating the airway and for adjusting the gas or vapor contents of the system and, finally, the use of the head low position are the basic requirements. It is of great importance, whatever type of machine is used, that there be little resistance in the airway. The simplest machine is that of Beecher,[13] which, with its few joints and therefore little tendency to leak, works very well for thoracic surgery. It is generally desirable to use it with two ether bottles in series or with one bottle and an ether "dropper."

ENDOTRACHEAL TUBES.—The use of endotracheal tubes is desirable in surgery through the open pleura. Such use appears indispensable for a low mortality rate in the group of cases in which pus or blood in the airway may be encountered during operation. We also believe that endotracheal tubes provide an indispensable safeguard in any operation in which the pleura may be accidentally opened, as in cardiac and pericardial operations, dorsal sympathectomy and substernal thyroidectomy. We now use tubes that lie free under an ordinary rubber face mask. Endotracheal tubes have two major functions in thoracic surgery, i. e., to ensure an open airway and the effective use of positive pressure when desired and to permit immediate and frequent bronchial aspiration when sputum or blood may obstruct the airway. Another function might be added, namely, that of abolishing cough by making closure of the glottis impossible.

During critical periods when a gush of purulent material may be thrown into the airway by manipulation of a diseased lung, or when bleeding into the airway may have occurred, the anesthetist is easily the busiest person on the team. Rapid, efficient bronchial aspiration may be of lifesaving importance. In patients who are under moderate cyclopropane anesthesia at such a time the anesthetic plane tends to become too light and to interfere with aspiration. This is not the case with ether.

Size.[14]—Discussion of the correct bore of the tube for endotracheal anesthesia has been common for a good many years. This has led to the use of increasingly large diameters, commonly up to 14 mm., and in some places even larger. Gillespie has rightly called this a vexed question. Perhaps the choice can be put on an objective basis by considering the function required.

The function of an endotracheal tube is, of course, to facilitate the ventilation of the lungs, and the measure of the effectiveness of this ventilation can in usual circumstances be judged by the oxygen saturation of the hemoglobin and the carbon

13. Beecher, H. K.: An Easily Transportable Apparatus for Anesthesia With or Without Compressed Oxygen, Especially Designed for Positive Pressure Anesthesia in Thoracic Surgery Under Military Conditions, War Med. **2**:602-608, 1942.

14. Beecher, H. K.: A Note on the Optimum Size of Endotracheal Tubes Based upon Blood Gas Studies, Anesthesiology **11**:730-372, 1950.

dioxide tension of the arterial blood. These should remain normal throughout prolonged anesthesia. As a generalization, one can say that the tube of smallest bore that will ensure this is the best.

Data obtained in connection with two other studies, when considered together, are relevant to this problem. In the first,[3] 43 patients who were undergoing thoracic operations were studied; among other things, arterial oxygen content and saturation of hemoglobin were measured. The satisfactory level of oxygen in the arterial blood is shown in table 1. In the second,[4] a careful study (uncomplicated conditions, patients supine, thorax not opened) of carbon dioxide content and tension and p_H of the arterial blood was made in 20 patients. The fixed acid increases were calculated. The studies were both made with the patients under ether anesthesia. The findings appear in table 2.

The endotracheal tubes used to obtain the data in table 1 were Flagg or Flagg-Woodbridge tubes, no. 7 or 9, or the Magill tube, size 32 French. Their maximum outside diameters are 11 mm. When the steel spring tubes were used, they were connected directly with the anesthesia machine through a Bradshaw rubber dia-

TABLE 2.—*Carbon Dioxide in Arterial Blood Serum* *

Number of Patients	Operations	Duration of Anesthesia, Open Drop No Endotracheal Tube (Min.)	Duration of Anesthesia, Closed with Endotracheal Tubes (Min.)	Before Anesthesia			Near Operation's End		
				p_H	CO_2 (Vol. %)	CO_2 Tension (Mm. Hg.)	p_H	CO_2 (Vol. %)	CO_2 Tension (Mm. Hg.)
10	Miscellaneous, patient supine	106	...	7.40	58.5	44.0 ± 0.7	7.38	54.8	41.5 ± 1.1
10	Miscellaneous, patient supine	...	124	7.40	60.0	42.7 ± 0.7	7.40	54.5	38.6 ± 1.0

* For further details see Beecher, H. K.: A Note on the Optimum Size of Endotracheal Tubes Based on Blood Gas Studies, Anesthesiology 11: 730-732, 1950.

phragm mask. The Magill tubes lay free under the face mask, without inflatable cuff or throat pack. Oxygenation, as shown, was satisfactory through both types of tube. The data on carbon dioxide in table 2 were obtained with Magill tubes, size 32 French; these lay free under the face mask and were used without cuff or throat pack. This, of course, permits some exchange around the tube. It is evident that there is no important difference in p_H, carbon dioxide content or carbon dioxide tension between the data obtained during open drop ether anesthesia without endotracheal tube and those obtained during the use of the closed machine (Foregger, circle filter) with the endotracheal tube (Magill, 32 French). An examination of each case record as well as of the average data shown here supports this statement. Individual case records as well as details of the technic of measuring the blood gases and p_H can be found in the papers referred to.

When one must deal with a large patient and the tube is to be connected directly with the anesthesia machine, a pharyngeal pack or inflatable cuff being used, it may be desirable to use a Magill tube, size 34 French but not larger. The 63 patients used in this study were adults chosen at random; they exhibited all the variation in size found in an ordinary hospital population. As already mentioned, surprisingly often one meets the point of view that as large an endotracheal tube

should be used as will slip through the cords. The skilled anesthetist can usually accomplish the insertion of large tubes without trauma; but however great the skill of the anesthetist, it is never great enough to prevent the trauma caused by the rubbing of the needlessly large tube against the tracheal mucosa with every breath the patient takes. Nor can it prevent the trauma that results from movement of the trachea by the surgeon. Then, too, the curve of the tube must fit the patient more precisely with large tubes than with small ones if trauma is to be avoided. The trauma on insertion increases directly as the skill of the anesthetist is deficient. Certainly less damage is caused by the smaller tubes, provided one uses a tube whose bore is adequate to provide for normal levels of oxygen and carbon dioxide in the arterial blood. As shown here, smaller tubes than generally supposed will provide these essentials.

Types: Magill Tubes: These rather soft rubber tubes are chiefly used in this clinic.

Flagg Tubes: Coiled wire spring tubes as modified by Woodbridge may be best when rapid bronchial aspiration may be necessary. However, we now rarely find them necessary.

Other Types of Endotracheal Tubes: Some tubes contain coiled wire springs permanently embedded in rubber. The tube wall is likely to be unjustifiably thick here. Plastic tubes are used in infants and small children.

Endobronchial Tubes: Several hazards are associated with the use of these tubes. Aside from the technical difficulties of their use and the possibilities for trauma during their insertion, they are likely to come out of place at inopportune times, even in the hands of those who are skilled in their use. This constitutes a serious hazard, for with them in place in the good lung it is difficult, if not impossible in many cases, to keep the area surrounding them free from pus, necrotic material and blood which may drain into it from the diseased lobe. If the endobronchial tube comes out of place, the good lung may be filled suddenly with this irritating, infectious material and the airway blocked by its quantity, whereas if this material is aspirated efficiently as it gathers, no such result occurs.

Even if these tubes could be held in place, their use is still contraindicated in many cases. If it is known with certainty before operation that an entire lung is to be removed, the use of an endobronchial tube inserted into the good lung in keeping that lung free from blood and irritating material may be at least theoretically sound. With this tube in place, considerable interference with aspiration of the diseased lung will be the case, with spread of irritating or infectious material throughout that lung. If the entire lung is to be removed, this spread makes no difference. If, during the course of operation, it is found to be unnecessary to remove the entire lung, any tissue which is then left in has been jeopardized, as well as the patient's life, for the inadequately aspirated, irritant, obstructing material has probably spread widely throughout the lung and it is likely that pneumonitis will develop in the remaining tissue.

The trauma from pressure on the mucosa of the bronchus of the good lung may be serious. Slough of tissue here can easily be fatal. (A number of fatalities are said to have occurred after slough of tracheal mucosa from the pressure of inflatable cuffs.)

Inflatable Cuffs: The routine use of an inflatable cuff on the endotracheal tube is not necessary [15] and is unwise for several reasons. Often rather profuse drainage from the diseased lobe will trickle into the trachea at a slow rate, so that it is impossible to pick up much of it by a catheter through an endotracheal tube. In the absence of the inflatable cuff much of this slow drainage follows along the outside of the endotracheal tube and drains into the face mask, since the patient is in the head-down position. In the presence of an inflatable cuff, a considerable quantity of this slow spillage may enter the good lung if it cannot escape alongside the endotracheal tube. With a short tube, the hazard from slow spillage would be avoided. An extremely short tube, however, would introduce other hazards and would not protect against sudden gushes of purulent material.

When gushes of purulent material suddenly enter the airway or a profuse endobronchial hemorrhage occurs, the speediest aspiration may not get all of it since the material cannot all enter the endotracheal tube. In the absence of an inflatable cuff, much will flow down alongside the endotracheal tube and out into the face mask, since the tube used here usually only about half fills the trachea. In the presence of an inflatable cuff this overflow material enters the good lung. We sometimes find that 2 or 3 ounces of pus and necrotic material have drained into the face mask during the course of a lobectomy for bronchiectasis, notwithstanding frequent bronchial aspiration.

It seems probable that inflatable cuffs sufficiently tight to hold a positive pressure of 20 cm. of water may damage the mucosa of the trachea or its delicate ciliary apparatus, making it ineffective at least temporarily for a period following the operation. Finally, several fatalities have been mentioned as resulting from the use of these tubes. Inasmuch as inflatable cuffs are unnecessary as a routine and even contraindicated in many cases, the fact that they have been demonstrated to have caused fatalities is a further argument against their use.

Pharyngeal Pack: When gastric distention is a problem or when it is anticipated as a consequence of the use of positive pressure in the airway, a pharyngeal pack around the endotracheal tube of a single long strip of gauze wrung out of isotonic sodium chloride solution may well provide a better solution of the problem than an inflatable cuff.

Bronchial Tamponage.—Various agents, such as rubber balloons and gauze packs, have been employed to close off the diseased lobe or lung in order to interrupt drainage therefrom. The principle of their use is sound, if the irritating, obstructing material can be confined to the region to be removed. In the case of lobectomy, the firm insertion of the tampon may be technically difficult and traumatic. Aside from technical hazards, the problem of ensuring its tight fit until the proper moment for removal is considerable, for if the pack becomes dislodged and unexpectedly releases a sudden flow of material into the airway, the result is likely to be unfortunate. The insertion of the pack to ensure its tight fit and yet

15. It might be expected that without an inflatable cuff around the endotracheal tube, gastric distention would result from the positive pressure employed in the airway. We have not found this troublesome except in esophageal surgery through the open chest when the esophagus was being tented up by the surgeon. Here the distention can often be relieved by a gastric tube opened at intervals; however, these esophageal and gastric operations are facilitated by the use of an inflatable cuff on the endotracheal tube or by the use of a pharyngeal pack. See section on transthoracic esophagectomy and gastric surgery.

easy removal at the proper time prolongs the wear on the patient before the induction of general anesthesia. Unless these tampons are nearly perfect, they are distinctly bad. It seems likely that the pressure one would necessarily have to use to hold them in place would inevitably produce major damage of the remaining mucosa. We have had no firsthand experience with them.

"CONTROLLED RESPIRATION."—It has been repeatedly advocated [16] that respiratory failure be produced by deliberate overventilation of patients under anesthesia and that this be followed by artificial ("controlled") respiration by the anesthetist. This is easier to accomplish with cyclopropane than with ether. The recommendation has been described as advisable chiefly for two reasons: first, in order that the operative field might be as quiet as possible, and, second, to ensure proper ventilation of the lungs, with avoidance of accumulation of carbon dioxide in the blood. For several reasons we do not believe that this technic is usually necessary or advisable: 1. An experienced surgeon is usually not seriously disturbed by the patient's respiratory movements, even in thoracic surgery, when the anesthesia is well conducted. 2. Crafoord's [17] data obtained from experiments on dogs suggested that a dangerous piling up of carbon dioxide might occur in the blood stream of patients when the pleura was open. This has also been taught by others. We have found in patients a great increase in carbon dioxide tension but not of carbon dioxide content. (See Beecher and Murphy.[3]) We believe that this problem can be handled better by "assisted" than by "controlled" respiration. 3. The deliberate production of respiratory failure in patients under anesthesia removes the greatest safeguard against overdosage. With the respiration eliminated, the anesthetist's first real warning of serious overdosage comes only at the time signs of circulatory failure are established. This is particularly unfortunate in the group of cases under discussion, for once circulatory failure begins, it is sometimes extremely difficult, if not impossible, to check it. 4. Several fatal explosions are said to have occurred when "controlled" respiration was maintained mechanically.

Aside from the cogent reasons just mentioned, we do not yet know that the alkalosis necessary for "controlled respiration" is compatible with safety in other

16. Guedel, A. E., and Treweek, D. N.: Ether Apnoeas, Anesth. & Analg. **13**:263-264, 1934. Waters, R. M.: Carbon Dioxide Absorption from Anæsthetic Atmospheres, Proc. Roy. Soc. Med. **30**:11-22, 1936.

17. Crafoord, C.: On the Technic of Pneumonectomy in Man, Stockholm, Tryckeri Aktiebologet Thule, 1938, p. 61.

In discussing pulmonary ventilation during thoracic surgery, Crafoord appears to give great weight to four experiments carried out in dogs. Three of these dogs were anesthetized with eunarcon, a barbiturate, and one with ether. It is now well known that barbiturates reduce the sensitivity of the respiratory center to carbon dioxide and, when the respiration is spontaneous, allow accumulation of carbon dioxide in the body. (See Beecher and Moyer, 1941, and many others.) In one experiment in a dog under ether, Crafoord found a considerable increase in carbon dioxide content. What the significance of this is it is impossible to say, since he did not determine the p_H, an indispensable measurement if one is to form any sound judgments as to the problem at hand. Nor did he measure the carbon dioxide–combining power in the ether experiment. The matter for chief concern is the carbon dioxide tension. The p_H is essential to a calculation of tension. Even if one were to accept this one experiment in a dog under ether as a guide, its irrelevancy becomes apparent when it is recalled that in 43 experiments in man Beecher and Murphy found no increase in carbon dioxide content, although the carbon dioxide tension rose to serious levels.

respects in the sick, often debilitated patients who must undergo thoracic surgery. There is some evidence that this procedure may result in a fall of blood pressure and increased strain on the circulatory system.

"Assisted Respiration."—As shown by Beecher and Murphy [3] in man, the carbon dioxide tension rises to dangerous levels with the passage of time during open thoracic procedures. The most effective ventilation can be given, we believe, by the anesthetist's squeezing the breathing bag as the patient starts a spontaneous inspiration. Nearly perfect synchronization can be obtained in this way, better than with a mechanical respirator. Even so, such assistance is not always effective, although it usually is.

PREANESTHETIC MEDICATION

Whichever anesthetic agent is chosen, its unpleasant or dangerous qualities can be minimized and induction facilitated by preanesthetic medication. Preanesthetic medication has four chief purposes in thoracic surgery.

1. It is desirable to ensure a restful night for the patient preceding operation and as much tranquillity as possible the day of operation. This is usually achieved with the use of pentobarbital sodium, 90 mg. by mouth, at bedtime, sometimes repeated once during the night. It is given again on waking the morning of operation. Since many of our surgeons prefer it, morphine sulfate, 10 mg., is often administered subcutaneously 45 minutes to an hour before anesthesia is to be started. There is no pharmacologic basis for this except the release from apprehension and the euphoria produced by the morphine. These qualities are greatly to be desired. The fact that they can be obtained as well with the doses of barbiturate mentioned is not widely enough recognized, nor is adequate attention given to the anorexia, nausea, vomiting and constipation often produced even by small doses of morphine.[18] The sedation should be achieved without producing respiratory depression, of course, not only because of the hazards of anoxia and elevation of carbon dioxide but also because reduction of respiratory minute volume will slow up the induction of inhalation anesthesia in a troublesome way.

2. It is important to minimize disturbing vagal reflexes once the anesthesia and operation have begun. To this end we customarily administer 0.6 mg. of atropine sulfate subcutaneously 45 minutes before induction of anesthesia, and, as mentioned in the section on vagal reflexes, atropine in 0.4 mg. dose is given intravenously if troublesome vagal activity is set off during the surgical procedure by mechanical stimulation of the pleura and lungs.

It is sometimes stated in an authoritative tone that such doses of atropine can have no important effect. The error of this statement is illustrated by the following case. The patient was a man in his middle thirties undergoing lobectomy for bronchiectasis. His pleura was inflamed and exceedingly sensitive, so that when it was stimulated by the surgeon's maneuvers great change in respiratory rhythm, rate and volume occurred. The heart rate was disturbed. Finally the operation was completed, and the chest drainage tube was placed on a negative pressure of 6 cm. of water. The patient immediately stopped breathing and became cyanotic. The

18. Denton, J. E., and Beecher, H. K.: New Analgesics: III. A Comparison of the Side Effects of Morphine, Methadon and Methadon's Isomers in Man, J. A. M. A. **141**:1148 (Dec. 17) 1949.

negative pressure was continued as long as we dared and then released. Respiration was resumed promptly in a normal way. After a few minutes, negative pressure was applied again to the pleural space and again the respiration was abruptly checked. The negative pressure was again released after the patient had become disturbingly cyanotic, and again spontaneous breathing recurred. After four repetitions of this sequence, atropine sulfate, 1.0 mg., was injected intravenously. The rather large dose of atropine was used because of the severity of the reflex phenomena. After a minute or two the negative pressure was applied to the chest tube as before; this time no interference with the respiration occurred. It seems reasonable to infer that the atropine was responsible for the good result.

3. Diminution of the secretion of saliva and mucus is desirable, for the stimulant or irritant action of the anesthetic agent needs to be opposed. The formation of saliva and mucus usually nearly or completely stops when a surgical level of general anesthesia has been attained. Repeated accumulation of secretions in the air passages at this time represents drainage of material deposited earlier in the terminal airways.

4. During intrathoracic surgery the heart is frequently exposed to mechanical trauma. For this reason we prefer to reduce the heart's sensitivity to stimulation by the administration of quinidine sulfate, 0.2 Gm. by mouth, the evening before operation and an hour and a half before the induction of anesthesia on the day of operation. When the use of this agent has been omitted from the preanesthetic medication and cardiac irregularities of the extrasystole type develop during the surgical procedure, quinidine lactate, 0.15 Gm., is given intramuscularly. Postoperatively quinidine sulfate is given four to six times in 24 hours in the doses mentioned for two or three days. (Subcutaneous injection will, curiously enough, result in a tender area and should be avoided. Quinidine should not be administered to a patient with a history of quinine sensitivity. Sensitivity to quinidine occurs once in about 1,500 patients.)

Procaine (2 per cent) has been painted on the surface of the heart to combat irregularities due to mechanical trauma. This measure may have some merit. Procaine given intravenously for the same purpose is of doubtful value. Irregularities which appear during cyclopropane anesthesia can be overcome by shifting to ether anesthesia.

CHOICE OF ANESTHETIC AGENT AND TECHNIC

INHALATION AGENTS.—It is our conviction that the hazards mentioned above can best be combated under inhalation agents. With ether and cyclopropane, there is great controllability coupled with the possibility of administering high oxygen tensions; in the case of the former agent there is a great factor of safety as well. Ether anesthesia at a depth great enough to produce respiratory failure leaves the circulation in good condition as long as anoxia is avoided. Intake of ether stops automatically before serious damage has occurred. Ether appears to be unique in this regard. The greater safety of this inhalation agent over the nonvolatile agent thiopental sodium (pentothal®) in patients who are poor risks was clearly shown in wartime.[19] All experienced surgeons and anesthetists who had a wide and long

19. Beecher, H. K.: Anesthesia for Men Wounded in Battle, Ann. Surg. **122**:807-819, 1945.

experience with severely wounded men were in agreement that those who were so badly wounded as to be in the "nontransportable" or field hospital category (as used in the Mediterranean Theater) would not stand the use of thiopental sodium but did tolerate the use of ether well. This lesson is applicable to the civilian patient undergoing thoracic procedures. Such patients are jeopardized by frequently decreasing circulating blood volume. This complication, we learned from experience, contraindicates the use of thiopental sodium but does not contraindicate the use of ether.

Ether Versus Cyclopropane: Many patients who undergo thoracic operations have a serious limitation of vital capacity. The procedures of the surgeon often tend to reduce further an already lowered vital capacity. There can be no question that the possibility of using a high percentage of oxygen with any desired depth of anesthesia is a characteristic of great value in anesthetic agents. Two agents in common use possess this qualification, ether and cyclopropane, although with ether it is possible to use about 15 volumes per cent more oxygen than with cyclopropane at the depth of anesthesia needed for operations around the hilus.

The strain on the circulatory system is considerably increased when the pleura is open to atmospheric pressure. This has already been discussed. The ideal anesthetic agent should not increase this strain. The tolerance for ether of patients with frank circulatory impairment is well established. It has also been well demonstrated that cyclopropane has a toxic effect on the heart in a relatively high percentage of patients. This toxicity is exhibited early in increased irritability of the heart, particularly undesirable when the heart may be exposed to mechanical trauma during the surgical procedure.

The final test in this regard must be made in the clinic. Although cyclopropane has been used at the Massachusetts General Hospital for many years (since 1935), we found that in a small number of thoracic cases the blood pressure began to fall gradually about an hour after induction. With ether, this "fatigue" usually did not appear until after three hours or more. A rather high incidence of low blood pressure following thoracic operations on patients under cyclopropane has also been observed and reported by Rovenstine.[20] It has been stated many times that bleeding is more profuse with cyclopropane than with ether, but objective proof of this is lacking.

As already shown, one of the great hazards in thoracic surgery is the rising carbon dioxide tension in the arterial blood. While Beecher and Murphy [3] have shown that this tension rises with ether anesthesia in the circumstances employed for thoracic operations in this clinic, Beecher, Francis and Anfinsen [4] have shown that the increase of carbon dioxide tension is not a property of ether anesthesia. It does not occur in patients who are supine, with closed chest. It is to be explained by the reduced ventilation concomitant with the position used and the open pleura. On the other hand, several investigators [21] have shown that a rise of carbon dioxide tension is the routine consequence of cyclopropane anesthesia, even when patients are not in the chest position and the pleura is not open. This is a decidedly objectionable quality for any agent to have when a thoracic procedure is to be carried

20. Rovenstine, E. A.: Cyclopropane in Thoracic Surgery, Anesth. & Analg. **14**:270-275, 1935.

21. Stormont, R. T.; Hathaway, H. R.; Shideman, F. E., and Seevers, M. H.: The Acid-Base Balance During Cyclopropane Anesthesia, Anesthesiology **3**:369-378, 1942. Beecher, H. K.: Unpublished data. Dripps.[9]

out. It seems curious that the "acidotic" qualities of cyclopropane have not been considered before as a valid objection to the use of the agent in thoracic procedures, during which, as already pointed out, the tendency of the carbon dioxide tension to rise as a consequence of the position and the open pleura must be combated. It is possible that this fact may have been responsible for the growing rejection of cyclopropane by experienced surgeons, a rejection based on bad results explicable on this basis.

Ether undoubtedly is more irritating to the mucous membranes than cyclopropane, although the latter agent is not without irritative effects, as shown, for example, by salivation and occasional laryngeal spasm. Salivation and the flow of mucus stop during full surgical anesthesia, so that these are a problem only during induction of anesthesia and recovery. Facilities for bronchial aspiration are essential, we believe, for several reasons; so if mucus is troublesome, it can easily be aspirated. During recovery, the cough reflex is usually present by the time the renewed secretion might cause difficulties. It is generally active by the end of the operation performed with the patient under ether.

Is the irritation caused by ether of importance in relation to morbidity or mortality? Information of value can be got from various sources. More and more information is accumulating which indicates that the anesthetic agent is not responsible for postoperative pulmonary complications in general surgery, e. g., the higher incidence in men than in women (2:1), the much higher incidence (2:1) of complications after upper abdominal operations than after lower abdominal ones and the equal incidence after general, local or spinal anesthesia as reported by several observers. In the course of many hundreds of thoracic operations with ether we hardly ever have seen the type of postoperative pulmonary complications found after gastric operations. A fairly wide experience with ether in the presence of active pulmonary tuberculosis, with good results, offers, in conjunction with the other points just mentioned, strong argument that the irritating quality of ether is not important in relation to morbidity or mortality.

Induction and recovery are slower with ether than with cyclopropane. Customarily, endotracheal tubes are placed in eight to 15 minutes when ether is used. The six or seven minutes that may be saved with cyclopropane hardly seem important. At the end of operation patients have their protective reflexes back about as soon as the dressings are completed, the drainage adjusted and the oxygen therapy, tent or nasal tube, arranged. Although bronchoscopy rarely must be carried out in the middle of a thoracic operation, when it is necessary the situation is often desperate. The procedure can be badly handicapped by the patient becoming too lightly anesthetized when under cyclopropane. This is not the case with ether. Fatal explosions appear to be commoner with cyclopropane than with ether.

Ether anesthesia, then, is our choice for major thoracic surgery. In most cases it is induced with nitrous oxide (80 volumes per cent) and oxygen (20 volumes per cent). Apprehensive patients are generally given thiopental sodium (usually about 0.2 Gm.), sometimes in their rooms for induction. In summary, our chief reasons for the use of ether are as follows: It is well tolerated even by the crippled circulatory system. An abundance of oxygen can be used with it (more than 95 volumes per cent, and it does not depress the respiration at levels which produced good muscular relaxation. When it is properly given, respiration is quiet; it does

not of itself produce respiratory acidosis, as does cyclopropane. The mortality rate from its use appears to be the lowest when compared with all other agents generally used for major surgery.

Vinyl Ether: This agent is used chiefly for the induction of anesthesia in young, excitable children. The open drop technic is employed.

Nitrous Oxide: Nitrous oxide is of value in inducing anesthesia in thoracic operations when it is possible to do so without producing clinical signs of anoxia. When the oxygenating power of the body has been crippled to the extent that the stage of surgical anesthesia cannot be entered under nitrous oxide without anoxia, skilful use of the agent still permits it to be of value in diminishing the irritant effects of ether, so that patients can be put under ether anesthesia without complaint or anoxia. Eighty volumes per cent nitrous oxide is useful for producing analgesia in conjunction with a local anesthetic or thiopental sodium. Nitrous oxide alone will not give an adequate depth of anesthesia for thoracic procedures.

NONVOLATILE AGENTS.—These agents have a desirable quality in that they are nonexplosive and noninflammable.

Tribromoethanol Solution U. S. P. (Avertin®): More than a dozen years ago this agent was frequently used as a "basal anesthetic" for thoracic surgery at the Massachusetts General Hospital. About that time it became apparent, with increasing experience, that even the so-called small basal doses (70 or 80 mg. per kilogram) would too often produce respiratory and circulatory depression in patients who were peculiarly liable to suffer from the results of such depression. An examination of our experience (about 4,000 administrations) with the agent in all cases indicated that even when the bad choices were eliminated the death rate was too high. It was found that the effects of this agent were not only highly undesirable but were also unnecessary. The use of tribromoethanol in thoracic cases was abandoned. In our opinion, the combination of this agent and nitrous oxide for use in thoracic operations can only be condemned. Direct reports from clinics where this combination is used support this conclusion.

Thiopental Sodium (Pentothal Sodium®): This agent has become well established and justly so for a wide variety of uses. It can be employed advantageously for the induction of anesthesia for thoracic surgery and in minor procedures. When the use of the cautery or diathermy knife is absolutely essential to extirpate a malignant growth this agent can be considered, but there its usefulness ends. Our conviction that it is unsuitable for major thoracic procedures is based on these reasons: It exerts its toxic effects chiefly on the respiratory and circulatory systems, the very systems that are most vulnerable in the group of cases under consideration. Curiously enough, subjects under barbiturate anesthesia react to positive pressure in the airway with apnea, as shown by Beecher and Moyer.[22] As already pointed out, patients undergoing thoracic surgery are, as far as their circulation is concerned, often comparable to men wounded in battle. The exceedingly poor tolerance of these men for thiopental sodium anesthesia has been established (Beecher[19]). Finally, a fairly extensive correspondence with anesthetists and surgeons gives factual evidence of frequent fatal accidents during thoracic operation on patients under this agent.

22. Beecher, H. K., and Moyer, C. A.: Mechanisms of Respiratory Failure Under Barbiturate Anesthesia (Evipal, Pentothal), J. Clin. Investigation **20**:549-566, 1941.

Thiopental Sodium (Pentothal Sodium®) and Curare: For some reason this combination of agents has achieved a wide use in thoracic surgery. The disasters caused by it are all too common, again judging from our correspondence. Furthermore, we have under way a five year study of these and other agents in a number of excellent university hospitals. At the end of the second year the record of this combination is distressing, to say the least. Publication of these data must wait three years more, until the numbers involved are adequate for a statistical review. Much casual data is far from reassuring. We believe that the only use for this combination in thoracic surgery is in the rare circumstances when cautery or diathermy must be employed.

Local Anesthesia.—Local anesthesia (1.0 per cent procaine hydrochloride) has established its value for use in minor thoracic operations, such as the drainage of empyema and lung abscess or thoracoscopy. We believe its use to be of value in blocking the vagus nerve and its pulmonary plexus, the phrenic nerve, or the heart's surface when troublesome responses arise from stimulation of these structures during thoracic operations on patients under general anesthesia. (Local block anesthesia is occasionally useful in diminishing postoperative wound pain.) The use of local anesthesia only in major open thoracic operations is subject to many of the same criticisms that can be applied to spinal anesthesia for this purpose. These are discussed below.

Spinal Anesthesia.—It was pointed out that anesthesia for open thoracic operations should be designed to overcome several hazards, including obstructing secretions, troublesome reflexes such as cough, anoxia and a rising carbon dioxide tension. None of these hazards can be as efficiently combated with spinal anesthesia as with general anesthesia. While an endotracheal tube can be introduced during topical anesthesia, difficulty may be experienced with it during spinal anesthesia in the long operations necessary in thoracic surgery, for the effects of topical anesthesia may disappear before the operation is completed. Without an endotracheal tube, the instantaneous and at times lifesaving bronchial aspiration will not be possible. Positive pressure anesthesia is likely to be less efficient without an endotracheal tube than with it. The use of positive pressure in the airway of a conscious patient is poorly tolerated.

Often a considerable point has been made of the maintenance of the cough reflex in patients under local or spinal anesthesia. An effective cough requires a tight chest wall, so that a high intrathoracic pressure can be built up. This is impossible during open thoracic work or after resection of ribs has mobilized a segment of the chest wall, and therefore such a cough cannot be efficient, as pointed out by Brown and Archibald.[2] As mentioned, cough has a spreading as well as an expulsive action. When the airway contains irritating infectious material, any attempt to cough may spread this to the lung tissue which is to remain.

The occasional crippling effects of high spinal anesthesia, as far as the respiration and circulation are concerned, are well known. Such interference is extremely undesirable. The statement sometimes made, and offered as an advantage, that little bleeding occurs (because of low blood pressure) during thoracic operations on patients under high spinal anesthesia requires no comment. If respiratory failure, hemorrhage or a fall in blood pressure occurs, it is more difficult to cope with it under spinal than under general anesthesia. Finally, the published mortality

figures for spinal anesthesia in thoracic surgery are anything but encouraging. We do believe, however, that there is sometimes a rare though legitimate use for spinal anesthesia when a bronchial fistula is present and cautery must be employed for a malignant process involving the chest wall. Even here the use of thiopental sodium or thiopental sodium and curare may be preferable. Probably a few lung abscesses could be operated on properly with the patient under light spinal anesthesia, provided the region for the spinal puncture was not heavily contaminated.

Topical Anesthesia.—Topical anesthesia is used to anesthetize the airway in the rare instances when an endotracheal airway is to be employed in conjunction with local or thiopental sodium anesthesia. Topical anesthesia sometimes must be used in order to carry out bronchoscopy after the end of a general anesthesia when this may have become too light. Cocaine 4 per cent or tetracaine hydrochloride (pontocaine®) 2 per cent is used.

The danger of tracheal and bronchial aspiration of vomitus is a definite hazard in patients who are under topical anesthesia. The conscious patient with proper instruction can assist in his own care. Patients who are under the influence of general anesthesia present a considerable hazard. On completion of the operation the patient should be placed in bed in the lateral position and the foot of the bed elevated 8 inches (20 cm.) or more. Constant nursing care should be provided until the topical anesthesia has disappeared and the reflexes of the larynx and trachea are active. With patients who have been thoroughly cocainized, this period of observation should continue at least two hours, until the topical anesthesia has worn off. For those who have received more superficial anesthesia induced by simply spraying the mucosa with a small quantity of topical anesthetic solution, an observation period of one hour is usually sufficient. During this period of observation nothing should be given by mouth. All vomitus and secretions should be carefully aspirated from the mouth and pharynx. Before constant nursing care is interrupted, the gag reflex should be tested and a normal response obtained.

FACILITATION OF THE SURGEON'S WORK BY THE ANESTHETIST

The anesthetist can make a difficult surgical job impossible; conversely, he can go far to lighten the surgeon's task not only by proper administration of inhalation anesthesia but by several maneuvers during the operation. The principal ones have been referred to. They will be gathered together and summarized briefly here. As pointed out, positive pressure wisely applied can do much to stabilize a swinging mediastinum. It can often be of great help in demarcating a section of lung during segmental lobectomy. In the lower lobes a clamp on the appropriate bronchiole will prevent distention of the segment in question, unless collateral respiration is effective. In many cases disease will prevent inflation of the segment to be excised when the lungs are inflated around it. In the upper lobes the segment is usually best shown by persisting inflation when the pressure is released.

"Assisted" respiration is frequently useful in smoothing out uneven respiration. In rare instances "controlled" respiration may be necessary and of help to the surgeon for a short time during intrathoracic procedures. These have been discussed in detail previously. During particularly trying vessel anastomoses, for

example, in linkage of the pulmonary and azygos veins, a quiet chest is necessary. With ether, fully controlled respiration is difficult to establish, so we give morphine, 6 to 8 mg. intravenously, and then gently assist the respiration while the anastomosis is under way.

Perhaps needless to say, the anesthetist should relieve the surgeon of any necessity for watchfulness of the patient's condition. He should inform the surgeon of all important untoward responses by the patient. The anesthetist is the guardian not only of the patient's airway and respiration but of his circulation as well, with responsibility for blood replacement. He keeps a watchful eye on all matters that concern the patient's welfare and are not a part of the operative procedure, for example, the room temperature, which should be maintained at about 75 F.

PROCEDURES AT THE END OF OPERATION

Several procedures are the responsibility of the anesthetist when the end of the operation approaches.

Inflation of the Lungs.—As the chest wall is closed, particular care should be taken to maintain the lungs in a fully expanded state until the chest wall is tight, usually until all except the skin sutures have been placed. A chest tube for drainage will usually have been sewn into the chest cavity. This should be closed off and finally aspirated by the surgeon to remove all air from the pleural space. As this aspiration is carried out, the anesthetist briefly increases the pressure in the airway. The anesthetist must be on the alert, particularly when the patient is moved, to recognize the sudden development of tension pneumothorax or collapse of a lung from obstruction. It is desirable to attach the chest catheter to a water seal bottle or to suction as soon as possible to avoid any possibility of tension pneumothorax.

Aspiration of the Airway.—The trachea and, so far as possible, the major bronchi should be aspirated with scrupulous care. It is important that the pharynx be cleared of any obstructing material before the endotracheal tube is removed.

Moving the Patient.—If the operating table has been "broken" in the middle, it should be flattened out as the closure of the chest wall is started, a half hour or so before the end of the operative procedure.

It is scarcely possible to overemphasize the importance of a slow, gentle, cautious handling of the patient during his transition from the operating position to his bed. The operation of lobectomy or pneumonectomy does not as a rule produce much disturbance in pulse rate or blood pressure. Occasionally, the circulatory system may show signs of strain in a falling blood pressure and a rising pulse rate. Even though the patient's condition may appear to be good, it must be assumed that he has suffered latent impairment of his circulation and that any further tax on the system will be followed by evidence of circulatory failure. To avoid further strain at the end of operation, the patient should be leveled slowly. This can be carried out during the last 15 minutes of the closure of the chest wall. While it is desirable to get the patient off his dependent, good lung and on his back, this must be done gently and with caution, for abrupt movement of a patient who has been long anesthetized results in too rapid redistribution of the circulating blood volume, with fall in blood pressure.

Oxygen Administration.—After removal of the anesthesia mask, the administration of oxygen is continued by means of a face mask and a breathing bag, with plentiful escape of gases so that the anesthetic agent can be washed out. The mask is used until the patient is returned to his room and installed in an oxygen tent in which a 50 per cent oxygen atmosphere is rapidly built up. (An oxygen flow of 10 liters per minute should maintain this.) Sometimes oxygen administered by nasal catheter is satisfactory. In this case 40 per cent oxygen in the inspired air is the usual achievement.

Bronchoscopy, For and Against.—Bronchoscopy as a routine at the end of a thoracic operation is neither necessary nor advisable. In the rare cases in which aspiration of the airway has failed to remove all foreign material and in which obstruction or unexplained cyanosis persists, it is sometimes necessary. Outside of the obvious indications for this procedure, there are several reasons for rejecting it as a routine. Patients have died during the procedure in many clinics. It seems unlikely that the bad results are all to be explained by ineptness on the part of those carrying it out. Perhaps they are to be explained in part at least by simple obstruction of the airway in a patient who has already built up a high carbon dioxide tension and who may have been suffering from anoxia for some time. There is evidence that tracheocardiac reflexes have produced fatalities. In order to perform bronchoscopy on a patient at the end of a thoracic operation, either the general anesthesia must have been kept undesirably deep for an undesirably long time, or it must be deepened at the end of a long and often trying procedure when the patient's circulatory stability already has been subjected to severe strain or the airway must be anesthetized topically. The hazards of this in a patient recovering from general anesthesia are great.

Finally, it must be borne in mind that bronchoscopy is no substitute for care in keeping the airway free of foreign material by repeated aspiration through the endotracheal tube. Bronchoscopy, in that it must be relatively brief, can care only for the material which has drained into the trachea or the major bronchi. Slow but continuous drainage from the terminal bronchioles can best be cared for by repeated aspiration through the endotracheal tube.

Postoperative Orders.—The postoperative orders should include a narcotic (morphine, 10 mg. subcutaneously every three hours, if needed for pain) and a sedative (phenobarbital sodium, 30 mg. every three hours, for restlessness, apprehension or "nervousness"). Quinidine lactate, 0.15 Gm., is given intramuscularly every four to six hours for two or three days. When possible quinidine sulfate is given by mouth in a dose of 0.2 Gm. Penicillin, 100,000 units, and streptomycin, 0.25 Gm., are given intramuscularly every six hours. Water is given by mouth in quantities up to 30 cc. per hour after nausea has passed. The pulse and blood pressure are observed and rceorded every quarter or half hour (depending on the patient's condition). Medium high head rest (up 12 inches [30 cm.] or so) is used when the patient is conscious, if his blood pressure is normal. Intravenous infusion of whole blood or 5.0 per cent dextrose in distilled water is given, depending on the patient's condition. The latter agent is generally limited to 1,500 cc. in the first 12 hours following operation. If the patient's blood pressure is not below normal, infusions should not run in faster than 50 drops per minute. Patients should lie on the side with the wound or on the back and be turned at

least every hour and encouraged to cough. The chest drainage tube is placed on "three bottle suction" (4 to 6 cm. of water). As indicated above, oxygen is given by tent or by nasal tube continuously from the time the mask is removed.

SPECIAL PROBLEMS ASSOCIATED WITH INFANTS AND SMALL CHILDREN

PREANESTHETIC MEDICATION.—All narcotics should be avoided in infants and small children. A barbiturate and atropine are the essentials. The elixir of pentobarbital is usually well tolerated by mouth in this group. If necessary the sodium salt of pentobarbital can be given subcutaneously or intramuscularly. Up to the age of 2 years, pentobarbital sodium is given in 5 to 20 mg. doses, depending on the size of the child. In this age range atropine sulfate, 0.15 to 0.3 mg., is given subcutaneously. In the 2 to 4 year old group, pentobarbital sodium, 15 to 40 mg. and atropine sulfate, 0.3 mg., are used. These doses are gradually increased with increasing age and size.

INDUCTION OF ANESTHESIA.—It is important to avoid heat loss, which occurs easily in the very young. The small child is best wrapped in a cotton (to avoid static sparks) blanket and held in the arms of a motherly nurse while induction of anesthesia is effected with vinyl ether and an "open drop" mask. This can usually be accomplished with about 10 cc. in 1 to 3 minutes. Ordinary ether is then given for 5 to 10 minutes, when the patient should be ready for intubation.

TRACHEAL INTUBATION.—Tracheal intubation is carried out under direct vision. A plastic tube is used. These tubes become troublesomely flexible with use and can be satisfactorily stiffened by immersion in cold water just before use. They are very flexible when warm, a desirable characteristic which should minimize trauma. Exceptional care must be taken to avoid trauma to the airway in these small patients, since edema of the trachea and pharynx as a response to trauma are particularly likely to develop in members of this age group. Tube sizes are no. 14 to 16 French for newborn infants. The tube must lie free in the trachea without pressure on the sides.

MAINTENANCE OF ANESTHESIA.—The endotracheal tube is connected directly with the anesthesia apparatus; anesthesia is maintained with ether vaporized by oxygen. (We have used cyclopropane for these patients but do not like it as well as ether.) It is essential to keep the dead space at a minimum. A pharyngeal pack can be used to prevent loss of gases and distention of the stomach. A single strip of gauze is wrung out of isotonic sodium chloride solution. One end is left protruding from the mouth at all times.

The anesthesia apparatus consists, in sequence, of an endotracheal tube and connector with an orifice where the anesthetic mixture enters, near the patient's face and between the patient and the soda lime canister. Excess cool gas mixture admitted through this orifice will spill out through the soda lime canister and help to keep it cool. Then, proceeding away from the patient, comes the carbon dioxide filter (180 Gm. of soda lime size, "to-and-fro" type) and the breathing bag (3 liter, light rubber type) with a "rat-tail" opening in the distal end into which a glass medicine dropper has been inserted. This allows for a steady escape of gases and is desirable for several reasons: (*a*) the chances for overdistention of the airway are reduced, (*b*) nitrogen or carbon dioxide from the patient is not allowed to accumulate in the system and (*c*) the extra flow of gases made possible by this vent helps to keep the system cool.

A face mask is rarely used on children under 7 years of age. In infants and small children the tidal volume is small in comparison to the minimum dead space of the apparatus. It is necessary to "assist" the respiration throughout the procedure by light pressure on the breathing bag. Generally it is enough to assist alternate breaths. Thus depth of anesthesia and condition can be judged from the patient's unassisted breath. (We find this system better than the Y tube arrangement, in which one arm of the Y is closed off by the anesthetist's index finger while pressure builds up in the infant's lungs and inflates them. The finger is removed and the lungs deflate.)

OTHER TRANSTHORACIC OPERATIONS

The general problems that arise during anesthesia for transthoracic surgery have been considered in the section on lobectomy and pneumonectomy. Special problems that are either peculiar to or are especially important in other transthoracic operations will be referred to briefly here.

CARDIAC SURGERY AND SURGERY OF THE GREAT VESSELS

When the disability which has caused the patient to seek medical assistance is such that pulmonary edema is one of the presenting signs, the anesthetist must make all possible efforts to guard against this serious complication. This is particularly likely to be present in patients with mitral stenosis. It is to be assumed, of course, that all possible medical measures such as the use of digitalis, diuretics and diet will have been taken, but the frequent ineffectiveness of these is well known. It is important that women with cardiac disease not be operated on at the time of their menstrual periods because of their tendency to store sodium and water at such intervals. Probably the worst risks to be encountered are the patients with mitral stenosis who come to the hospital for azygos-pulmonary vein anastomoses to relieve their pulmonary hypertension. Even slight agitation is sufficient to precipitate an attack of pulmonary edema.

Apparently the psychic trauma associated with operations on the heart or the great vessels is severe. Accordingly, the need for accurate and effective preanesthetic medication is important. Of especial value are repeated small doses of barbiturates. As described previously, the use of quinidine is important. Notwithstanding the general undesirability of using thiopental sodium (pentothal®) in patients with cardiac disease, we have found it advisable to put these patients to sleep in their rooms with small doses of the barbiturate and thus to prevent the apprehension and agitation which may characterize patients who are to undergo cardiac operations. A brief nitrous oxide-oxygen induction, with never less than 25 to 30 per cent oxygen, is followed by ether and oxygen for maintenance.

At the time when the vascular anastomosis is to be carried out it is of the utmost importance to have quiet respiration. For reasons given earlier, we prefer to use ether anesthesia for these patients. Quiet respiration can be ensured for this period by the intravenous injection of 8 to 10 mg. of morphine in adults and a correspondingly smaller dose for children.

Cardiolysis for constrictive pericarditis is carried out with the patient semirecumbent on an operating table or tied into a dentist's chair and under endotracheal ether anesthesia.

Particular care must be taken with these groups of patients not to overload the circulation with either blood or electrolytes.

THYMECTOMY FOR MYASTHENIA GRAVIS

It is assumed that operation on patients with myasthenia gravis will not be contemplated during any period of infection, nor for two or three months after an infection. Infections of the upper respiratory tract are common and often fatal in this disease, as emphasized by Blalock.[22a]

About 45 minutes before induction of anesthesia is to start, 1.5 to 2.5 mg. of neostigmine methylsulfate (prostigmin methylsulfate®)[23] and 0.6 mg. of atropine are given subcutaneously. Repeated doses of neostigmine and atropine may be necessary at about two hourly intervals during the surgical procedure, as indicated by respiratory depression or the accumulation of secretions in the airway. It must be remembered (but too often is not) that when the peripheral circulation closes down, as it is likely to do in these patients, and the skin becomes cold, the subcutaneous injection of these agents will not be adequately absorbed and no effect occurs. The foolish use of several subcutaneous or intramuscular injections can have serious consequences, if the patient survives, when his peripheral circulation is later restored, for then all the injections may be absorbed at once, with a toxic effect. In circumstances in which the peripheral circulation is greatly reduced it is better to give the injections intravenously. It is urgent that the anesthetist work with great care, avoiding trauma and maintaining a clean airway through the endotracheal tube so that postoperative infection can be avoided.

We have carried out anesthesia in a considerable number of these patients under ether but in the last few years have used cyclopropane chiefly because of the rapidity with which the agent is eliminated and normal function of the respiratory muscles, or as near normal as possible, can be reestablished. Whether the patients do better under cyclopropane than under ether has not been settled. Possibly they do.

Postoperatively it is important that the foot of the bed be elevated 10 or 12 inches (25 to 30 cm.) and the patient guarded constantly against aspiration of gastric contents until he is fully conscious.

22a. Blalock, A.; Harvey, A. M.; Ford, F. R., and Lilienthal, J. L., Jr.: The Treatment of Myasthenia Gravis by Removal of the Thymus Gland, J. A. M. A. **117**:1529-1533 (Nov. 1) 1941.

23. Some surgeons prefer the following regimen. Patients with myasthenia gravis receive their usual oral prostigmin® medication up to one hour before anesthesia is to be induced. For the correct intravenous dose, calculate that 0.5 mg. of prostigmin methylsulfate® is equivalent to 10 to 15 mg. of prostigmin bromide® administered orally. The 24 hour dose of prostigmin methylsulfate® is estimated on this basis. One third of this is added to 1,000 cc. of 5 per cent dextrose in distilled water and the intravenous infusion started one hour before operation. The rate of inflow is adjusted so that administration of this third of the daily requirement will be completed in eight hours.

Here other premedication consists of pentobarbital sodium, 0.1 Gm. by mouth, one and one-half hours before anesthesia, and atropine sulfate, 0.6 mg. subcutaneously, one-half hour prior to anesthesia. It may sometimes be desirable to give additional pentobarbital sodium in a small dose (30 mg.) intravenously. Usually no additional atropine is necessary. If excessive mucus collects in the airway, 0.2 mg. of atropine sulfate is given intravenously and 0.4 mg. subcutaneously. Postoperatively the intravenous drip of prostigmin methylsulfate® is adjusted to the needs of the patient. Patients are usually able to take oral medication within 24 hours.

TRANSTHORACIC ESOPHAGECTOMY AND GASTRECTOMY

The problems in transthoracic esophagectomy and gastrectomy differ little from those already described for lobectomy and pneumonectomy. Patients who undergo this type of surgery should have a Levin tube placed in the stomach. This is aspirated steadily throughout the operation. Here again, nitrous oxide–oxygen induction of ether anesthesia is used. In this group of patients some trouble may arise from distention of the stomach when positive pressure is used. This complication can be avoided by the use of inflatable cuffs or preferably a pharyngeal pack.

If the surgeon does not wish to still the diaphragm by crushing the phrenic nerve, block of this nerve under direct vision with 1.0 per cent procaine hydrochloride will facilitate the procedure. In operations on esophageal diverticula, whenever barium sulfate has been used for roentgenologic study in the weeks preceding surgical intervention patients should be subjected to laryngoscopy before the endotracheal tube is withdrawn at the end of operation and any barium sulfate chunks present in the pharynx removed, lest they obstruct the airway.

DRAINAGE OF LUNG ABSCESS

Drainage of lung abscess is usually undertaken with local block anesthesia. Whenever lung tissue must be cut across, it is important to have the patient's head and chest lowered to increase the pressure in the pulmonary circulation and thus to minimize the possibility of air emboli.

THORACOPLASTY

A prejudice exists against the use of ether anesthesia for operations on tuberculous patients. Where this originated is uncertain, but the current basis for it can be found in numerous published statements. On examination, these statements do not appear to be founded on study and careful record keeping; casual opinion appears to have served as the basis for many of the statements voiced against ether. Three groups of workers have in the past attacked the problem experimentally, and not one was able to substantiate the prejudice against the use of ether anesthesia. Most of the articles which apparently serve as the basis for the current prejudice against ether were written from one to three decades ago and were based on observations of "open cone" or "open drop" ether administration. It is probable that some of the secondary results of the use of this technic are as undesirable in the presence of pulmonary tuberculosis as they are in the presence of other conditions.

Since the prejudice against the use of ether anesthesia for operations on tuberculous patients does not appear to be based on a secure foundation and since, as far as we have been able to find, no extensive clinical study of this matter has been carried out, we have for many years been using closed ether anesthesia (with carbon dioxide absorption) in operations on consecutive patients undergoing surgical treatment of their pulmonary tuberculosis.[24]

The choice of operating time is in the afternoon after elimination of the morning sputum. Preanesthetic medication is like that described for the lobectomy-

24. Beecher, H. K., and Adams, R.: Ether Anesthesia in the Presence of Pulmonary Tuberculosis, J. A. M. A. **118**:1204-1209 (April 4) 1942.

pneumonectomy group of operations. Patients are placed in position for operation before anesthesia is induced. During induction, care is taken to avoid straining and coughing. Anesthesia is administered by means of a closed system apparatus with carbon dioxide absorption (never the open cone for these patients). After a brief nitrous oxide–oxygen induction, with care to avoid anoxia, ether anesthesia is administered with a high percentage (95 volumes per cent) of oxygen. Although endotracheal tubes are used with great frequency in this hospital and are always used in operations on the open pleura, we use them in the presence of pulmonary tuberculosis only when the sputum is unusually abundant. We are reluctant to use them in most cases of tuberculosis, for possibly new loci of tuberculous infection might develop in areas of slight trauma to the airway. During operation the patient is maintained in a slight Trendelenburg position to promote drainage.

Our data include all cases, favorable and unfavorable. The surgical teams are constantly changing, the surgeons varying from members of the house staff to the chief of service. Notwithstanding these facts, our results compare well with those from other clinics where ether is used either not at all or rarely.

In our opinion, the anesthetic agent is not important in these cases as long as it permits the use of a plentiful supply of oxygen and allows the surgeon to carry out a deliberate, unhampered and unhurried operation, provided the patient is not jeopardized by toxic action of the anesthetic. It is important to choose an anesthetic agent which depresses vagal activity when a thoracic operation is contemplated. Ether apparently is better than other agents studied in this regard. The excellent tolerance of the very sick patient for ether anesthesia as well as the low death rate attributable to this agent are well established. After a good many years of use we can see no reason to abandon ether in operations on the tuberculous patient because of the presence of tuberculosis.

AUREOMYCIN THERAPY IN LYMPHOGRANULOMA VENEREUM

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AFTER the definition of lymphogranuloma venereum as a clinical entity in 1913 [1] and the development of a diagnostic skin test in 1925,[2] the disease received wide recognition and numerous therapeutic agents were used in attempts to cure it. Indifferent results were obtained until the advent of sulfanilamide, which proved encouraging in the experience of early investigators.[3] Although later reports of the cumulative experience were less optimistic,[4] administration of the sulfonamides remained the treatment of choice, since some virustatic properties were demonstrated and secondary infection was controlled. Penicillin showed slight promise,[4a, d] and streptomycin has had little clinical trial.

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1. Durand; Nicolas, J., and Favre, M.: Lymphogranulomatose inguinale subaiguë d'origine génitale probable, peut-être vénérienne, Bull. et mém. Soc. méd. d. hôp. de Paris **35**:274-288, 1913.

2. Frei, W.: Eine neue Hautreaktion bei "Lymphogranuloma inguinale, Klin. Wchnschr. **4**:2148-2149, 1925.

3. Knight, A. A., and David, V. C.: The Treatment of Venereal Lymphogranuloma with Sulfanilamide, J. A. M. A. **112**:527-529 (Feb. 11) 1939. Levy, J. G.; Holder, E. C., and Bullowa, J. G. M.: Stricture of the Rectum Due to Lymphogranuloma Venereum: Symptoms and Treatment with Sodium Sulfanilyl Sulfanilate, Am. J. Digest. Dis. **9**:237-239, 1942. Marino, A. W. M.; Buda, A. M.; Turell, R., and Nerb, L.: Treatment of Venereal Lymphogranuloma with Sulfanilamide, Am. J. Surg. **46**:343-347, 1939. Schamberg, I. L.: The Course of the Plasma Protein Changes in Early Lymphopathia Venereum Under Treatment with Sulfanilamide, Am. J. M. Sc. **201**:67-81, 1941. Seidenstein, H. R.: Rectal Stricture Due to Lymphogranuloma Venereum; Treatment with a Sulfonamide and Frei Antigen, Surgery **14**:73-82, 1943.

4. (*a*) Greenblatt, R. B., and Wermer, P. L.: Lymphogranuloma Venereum, M. Clin. North America **29**:663-687, 1945. (*b*) Koteen, H.: Lymphogranuloma Venereum, Medicine **24**:1-69, 1945. (*c*) Woods, F. M., and Hanlon, C. R.: Inflammatory Stricture of the Rectum: Analysis of 192 Cases, Including 35 Treated by Rectosigmoid Resection, Ann. Surg. **120**:598-606, 1944. (*d*) Wright, L. T.; Freeman, W. A., and Bolden, J. V.: Lymphogranulomatous Strictures of Rectum: Résumé of 476 Cases, Arch. Surg. **53**:499-544 (Nov.) 1946.

The discovery of aureomycin [5] and the demonstration of its activity against rickettsias and certain virus infections [6] led to the early clinical trial of this agent in the treatment of lymphogranuloma venereum by Wright and his associates.[7] They reported the early results in the treatment of 35 patients with lymphogranuloma venereum, 12 with buboes, 5 with proctitis and 18 with rectal stricture. Treatment was by the intramuscular injection of aureomycin in a daily dose of 10 to 40 mg. for a period of 10 to 50 days. Marked improvement in all cases was observed at the time of completion of treatment. Follow-up observations on 14 patients indicated an apparent relapse in one case of proctitis and in two cases of rectal stricture.

Encouraged by this report, we undertook to study the treatment with aureomycin of a small group of patients with lymphogranuloma venereum. The following objectives were proposed: (1) to study the effectiveness of aureomycin when administered orally; (2) to observe the clinical course of the patients for a period of months after treatment; (3) to study the effect of treatment on the persistence of complement-fixing antibodies in the blood serum.

TABLE 1.—*Classification of Lymphogranuloma Venereum Infections*

	Number of Patients
Acute inguinal adenitis	3
Proctitis without stricture	2
Rectal stricture without colostomy	7
Rectal stricture with colostomy	7
Total	19

This study has now been in progress for over a year, and a preliminary report of our observations seems warranted.

MATERIAL AND METHODS

Nineteen patients with a clinical and laboratory diagnosis of lymphogranuloma venereum were available for study and treatment. The patients were classified according to the types of disease, divided into four: acute inguinal adenitis, proctitis without stricture, rectal stricture without colostomy and rectal stricture with colostomy (table 1). In each instance the diagnosis was established by the characteristic clinical picture based on history, physical examination and proctoscopic examination and a positive reaction to the complement fixation test with the lymphogranuloma venereum antigen. The Frei test was avoided because of its

5. Duggar, B. M.: Aureomycin: A Product of the Continuing Search for New Antibiotics, Ann. New York Acad. Sc. **51**:177-181, 1948.

6. Anigstein, L.; Whitney, D. M., and Beninson, J.: Aureomycin: A New Antibiotic with Antirickettsial Properties; Its Effect on Experimental Spotted Fever and Epidemic Typhus, Ann. New York Acad. Sc. **51**:306-317, 1948. Wong, S. C., and Cox, H. R.: Action of Aureomycin Against Experimental Rickettsial and Viral Infections, Ann. New York Acad. Sc. **51**:290-305, 1948.

7. (*a*) Wright, L. T.; Sanders, M.; Logan, M. A.; Prigot, A., and Hill, L. M.: Aureomycin: A New Antibiotic with Virucidal Properties: I. A Preliminary Report on Successful Treatment in 25 Cases of Lymphogranuloma Venereum, J. A. M. A. **138**:408-412 (Oct. 9) 1948; (*b*) The Treatment of Lymphogranuloma Venereum and Granuloma Inguinale in Humans with Aureomycin, Ann. New York Acad. Sc. **51**:318-330, 1948.

possible effect on subsequent complement fixation tests. In 10 instances, however, a positive reaction to the Frei test had been obtained before the patient was referred to us.

Routine laboratory studies carried out in all cases included hemoglobin determination, white blood cell count, serologic test for syphilis and determination of the albumin-globulin ratio of the serum. The protein fractionation was performed by the modified salting-out method of Rheinhold.[8] Biopsy material from 10 of the patients with rectal stricture was submitted for histological diagnosis. Specimens of the rectal mucosa from three patients with rectal stricture were obtained for attempts at virus isolation. In five instances aspiration biopsy of the liver was performed and the tissue submitted for histological study and for attempted isolation of the virus.

The study and treatment of the patients were carried out in the surgical wards and in the surgical outpatient clinic of the University Hospital. At first we followed the plan of treatment used by Wright and his associates,[7a] giving small doses of aureomycin intramuscularly. Four patients received 20 mg. daily for 10 days by intramuscular injection, and one patient received 80 mg. daily for seven days. All these patients except the last mentioned later received additional oral therapy. Oral dosage at first consisted of 2.0 Gm. daily for seven days. Later this dosage of the drug by mouth was continued for 28 days. Nausea and vomiting made it necessary to limit some patients to 1.0 Gm. daily and caused others to discontinue treatment altogether. For these reasons there was a considerable variation in the treatment received by individual patients. The total dosage of aureomycin received by each patient is indicated in tables 2 and 3.

All patients have been closely followed up to the present time, the periods of observation varying from two to 14 months. Follow-up observations have included inquiry as to symptoms, repeated digital or proctoscopic examinations of the rectum, repeated determinations of the complement fixation reaction and determination of the albumin-globulin ratio of the serum.

The complement fixation tests were performed as follows: Twofold dilutions of serum, in 0.1 cc. amounts, were mixed with 0.1 cc. of a 1:4 dilution of lygranum [9] antigen and 0.2 cc. of complement containing 1.5 to 2.0 units. The test tubes were kept overnight in the refrigerator. Then 0.2 cc. of sensitized red cells (0.1 cc. of 2 per cent sheep red cells and 0.1 cc. of appropriately diluted hemolysin) was added to all tubes, and they were incubated for 30 minutes at 37 C. The titers, which represent initial dilutions of serum, are based on 3+ or 4+ complement fixation. Each serum was also tested with a normal yolk sac preparation supplied with the lygranum antigen as a control.

CLINICAL RESULTS

Acute Inguinal Adenitis.—Three patients with acute inguinal adenitis caused by lymphogranuloma virus were treated with aureomycin. All were young men with a negative reaction to the serologic test for syphilis, and the symptoms were of relatively short duration. All had a positive complement fixation reaction with the lymphogranuloma antigen. In all three instances the buboes subsided

8. Rheinhold, J. G.: To be published.

9. Lygranum was obtained from E. R. Squibb and Sons.

promptly within two weeks after the initiation of treatment with aureomycin. These patients have been followed for eight to 11 months after treatment. One patient (F. M.) who was treated with small intramuscular doses of aureomycin had a mild recurrence of adenitis two weeks after treatment. The other two have remained free of symptoms, and examination shows only small "shotty" inguinal lymph nodes. These two patients showed a marked and progressive fall in the titer of complement-fixing antibodies following aureomycin therapy. The third (F. M.) showed only an equivocal decrease, but we do not know how high his titer might have gone up between the far-spaced times that blood was taken.

Proctitis.—A diffuse proctitis without stricture formation was encountered in two patients. Both were women, one 42 years of age and the other 30. One of these patients was treated with aureomycin on two occasions. The other was treated with chloromycetin® and did not receive any aureomycin.

Both patients had a positive reaction to the complement fixation test for lymphogranuloma, and one (E. S.) had reacted positively to the Frei test on several occasions prior to this study. The Frei test was not done in the case of L. S. The chief complaints of both patients were diarrhea, abdominal cramps and rectal bleeding. Proctoscopic examination showed no stricture, but the rectal mucosa for a distance of 10 to 15 cm. was red, granular and edematous and in one case showed superficial ulceration. Biopsy of the mucosa showed a nonspecific proctitis.

The first patient (E. S.) had had the symptoms mentioned intermittently for seven years and had been examined and treated in the Medical Wards of the University Hospital in 1942 and 1944. On her second admission the diagnosis of lymphogranuloma proctitis had been made on the basis of a positive reaction to the Frei test and she had responded well to a course of sulfanilamide therapy. At the time of the present admission she was having two to three bowel movements daily and bright blood was apparent in the stools. Within two days after the start of aureomycin therapy, 20 mg. intramuscularly daily for 10 days, the stools were free of blood and she was having one normal bowel movement every day or two. Proctoscopic examination revealed considerable improvement in the appearance of the rectal mucosa. Complete relief of symptoms persisted for five months, but then rectal bleeding and mild diarrhea recurred. Proctoscopic examination showed a red and edematous mucosa with multiple pinhead, superficial ulcerations. Another course of aureomycin (1.0 Gm. daily by mouth for 28 days) had little immediate effect on the disease, although there has been some gradual improvement in the five months which have elapsed since then. It is difficult to evaluate the results of aureomycin therapy in this case. Certainly the immediate response to the first course of treatment was dramatic, similar to the results reported by Wright.[7]

The other patient (L. S.) had a known illness of only one year's duration. In the last three to four months there had been a weight loss of 24 pounds (11 Kg.) and a feeling of fatigue and lassitude. She was treated with chloromycetin,® 3 Gm. daily by mouth for 28 days, a total of 84 Gm. This patient has been observed for a period of only two months, but she feels much stronger, has lost no more weight, diarrhea has ceased and rectal bleeding has greatly diminished, although it is still occasionally present. This result could have been considered encouraging; however, proctoscopic examination now shows some narrowing of

TABLE 2.—*Rectal Stricture Without Colostomy*

Patient	Age Race Sex	Duration, Yr.	Before Treatment: Symptoms	Before Treatment: Rectal Lesion	Pathologic Condition	Period of Observation, Mo.	Total Dosage	After Treatment: Symptomatic	After Treatment: Rectal Lesion	Weight Gain, Lb.	A/G Ratio: Initial	A/G Ratio: Final	Complement Fixation: Initial	Complement Fixation: Final
S. P.	39 N F	3	Rectal bleeding, constipation, fatigue	Stricture at 3 cm., diameter 0.5 cm.; tender	Proctitis	10	Oral, 64 Gm.	No rectal bleeding; bowels normal; feels stronger; gaining weight	Stricture diameter increased to 1 cm.; no tenderness	6	2.7/4.8	3.5/5.2	640	320
A. L.	42 N M	1	Constipation, abdominal cramps, weight loss	Stricture at 3 cm., diameter 0.5 cm.; not tender	Granuloma	9	Oral, 70 Gm.	Bowels normal; gained 9 lb.; feels fine	Stricture unchanged	9	2.2/8.0	2.7/6.5	640	320
M. B.	64 N F	10	Constipation, abdominal distention, rectal bleeding	Stricture at 2 cm. and 8, diameter 0.6 cm.; tender	Granuloma	8	Oral, 70 Gm.	Obstruction became complete after treatment; colostomy performed; perianal abscess	Stricture unchanged; still tender	0	1.2/4.8	1.3/6.8	160	320
H. B.	33 N M	5	Wound unhealed after fistulectomy, rectal bleeding, purulent discharge, constipation	Granulating wound, right buttock; stricture at 5 cm., diameter 1.5 cm.; tender	Granuloma	7	Oral, 88 Gm.	No rectal bleeding or purulent discharge; bowels normal	Wound healed; induration but no stricture; no tenderness	0	1.9/7.2	2.8/6.8	1,280	1,280
N. F.	34 N F	½	Constipation, abdominal cramps, weight loss, 15 lb.	Stricture at 2 cm., diameter 0.5 cm.; tender	Granuloma	7	Oral, 80 Gm.	Mild constipation; gained 9 lb.; feels well	Stricture unchanged; less tender	9	2.7/5.3	3.6/5.6	80	80
M. Br.	28 N F	2½	Constipation, abdominal distention, foul rectal discharge, weight loss	Stricture at 3 cm., diameter 0.3 cm.; tender	Proctitis	5	Oral, 40 Gm.	Obstruction became complete during treatment; colostomy performed; not much improved	Stricture unchanged; still tender	30 after colostomy	1.6/5.6	2.8/5.6	160	160
L. P.	31 W F	2	Perianal abscesses, constipation	Stricture at 5 cm., diameter 1.5 cm.; tender; anal fistula	Proctitis	6	Oral, 28 Gm.	Bowels move more freely; feels well; gaining weight	Stricture diameter increased; still tender	10	.....	3.2/5.0	640	640

the lumen at 4 to 5 cm. suggesting early stricture formation. In this single case the clinical response to treatment with chloromycetin® was similar to the results obtained with aureomycin.

Rectal Stricture Without Colostomy.—There were seven patients in this group. The clinical and laboratory data are summarized in table 2. Two of the patients were men and all except one were of the Negro race. The apparent duration of the disease was 10 years in one case, but in all others it was less than three years. All patients complained of increasing constipation. Four patients complained also of abdominal cramps or distention, four of rectal bleeding or purulent discharge, three of weight loss and two of perirectal infections. In each instance proctoscopic examination revealed a definite stricture 3 to 5 cm. above the anal orifice. The stricture was usually tender. Biopsy of the strictured area was reported to show granuloma of the rectum or nonspecific proctitis in each instance. The treatment of all the patients was by the oral administration of aureomycin, the total dose for each patient varying from 28 to 70 Gm.

Two of the patients (M. B. and M. Br.) showed abdominal distention and definite signs of partial obstruction of the large bowel when they were first seen. Ordinarily a colostomy would have been done at once, but it was decided to investigate the possible beneficial effect of aureomycin therapy. The first patient (M. B.) was much improved after the first course of oral therapy (14 Gm.). Abdominal distention diminished, bowels moved regularly and she gained weight. Three months later, after an additional course of 56 Gm. of aureomycin, obstruction occurred once more and a sigmoid colostomy was done. The rectal stricture remained tight and tender five months after the use of aureomycin was discontinued. The other patient (M. Br.) had complete obstruction, and colostomy was required at the time that aureomycin was being administered. She had received 28 Gm. of aureomycin. Since then she has had more aureomycin to a total of 40 Gm. and has gained 30 pounds (13.6 Kg.). The stricture was still tight and tender months after administration of aureomycin was discontinued. At present we have no evidence that aureomycin was of value in the treatment of these two patients.

The remaining five patients showed a more encouraging response to treatment. Rectal bleeding and purulent discharge ceased promptly, bowel function was greatly improved and the patients began to gain weight. At the end of an average period of observation of eight months only one patient still complained of mild constipation. The other four had normal bowel habits and all except one had shown a notable gain in weight, an average of 8 pounds (3-6 Kg.) in the four cases. All the patients feel well and are carrying on their normal activities.

Examination of the rectum revealed a definite increase in the diameter of the stricture in three of these five patients. Tenderness disappeared in two instances, persisted in two and was not present initially in one. In general the objective improvement was somewhat less striking than the symptomatic relief afforded.

Rectal Stricture with Previous Colostomy.—The group of patients with this condition numbered seven, all Negro women, whose ages ranged from 29 to 68 (table 3). The symptoms of all patients were of long duration, varying from nine to 13 years. Only one of the patients (M. M.) had a positive reaction to the serologic test for syphilis. In each instance a colostomy had been performed previously because of obstruction due to the rectal stricture, and in general the

TABLE 3.—*Stricture with Colostomy*

Patient	Age Race Sex	Duration, Yr.	Symptoms	Rectal Lesion	Pathologic Condition	Period of Observation, Mo.	Total Dosage	Results		A/G Ratio		Complement Fixation	
								Symptomatic	Rectal Lesion	Initial	Final	Initial	Final
A. H.	29 C F	10	Colostomy; slight itching and rectal discharge	Stricture at 3 cm.; diameter 0.2 cm.; moderately tender	Granuloma	12	I.M., 200 mg. Oral, 56 Gm.	Rectal discharge and pruritus	Stricture unchanged; still tender	5.0/2.6	3.5/4.6	320	320
B. W.	68 C F	12	Colostomy; no rectal symptoms	Stricture at 1 cm.; lumen closed	.....	12	I.M., 200 mg. Oral, 10 Gm.	"Feels better"	Stricture unchanged	3.7/4.4	2.9/5.8	160	320
A. L.	43 C F	12	Colostomy; slight rectal soreness and discharge	Stricture at 1 cm.; diameter 0.3 cm.; tender	.....	11	I.M., 200 mg. Oral, 56 Gm.	No rectal discharge; "feels better"; weight gain	Stricture unchanged; less tender	2.7/4.1	3.6/4.1	80	160
M. B.	48 C F	10	Colostomy; no rectal symptoms	Stricture at 1 cm.; diameter 0.1 cm.; not tender	Granuloma	11	Oral, 28 Gm.	No change	Stricture unchanged	2.5/4.6	3.2/5.9	80	80
G. D.	37 C F	9	Colostomy; foul rectal discharge	Stricture at 1 cm.; lumen 2 mm.; moderately tender	.....	11	Oral, 39 Gm.	No change, still has rectal discharge	Stricture unchanged; still tender	3.3/4.4	.....	80	80
M. M.	47 C F	13	Colostomy and right colectomy	Stricture at 2 cm.; lumen closed; slightly tender	.....	10	Oral, 34 Gm.	No change	Stricture unchanged	2.7/5.7	3.6/5.3	160	160
E. D.	.. C F	11	Colostomy; slight rectal pain and discharge	Stricture at 2 cm.; lumen 4 mm.; tender	.....	9	Oral, 64 Gm.	Discharge less; "feels better"; weight gain, 15 lb.	Stricture unchanged; still tender	2.9/5.5	3.1/5.2	320	320

rectal symptoms at the time of this study were mild. Three patients described a slight rectal discharge, and one complained of a fairly troublesome foul discharge. Three also complained of mild pain or soreness in the rectal area, and three would admit to no rectal symptoms. On examination the strictures were found to be firm and fibrotic, with a very small lumen. In two instances the lumen appeared to be completely obliterated. Some degree of tenderness was noted by five of the seven patients. Biopsy of the stricture in two instances showed the histological picture of granuloma of the rectum.

Three of the seven patients were treated initially by the intramuscular injection of 20 mg. of aureomycin daily for a period of 10 days. All of these subsequently received additional oral treatment, and the other four were treated entirely by the oral route, the total dosage of aureomycin varying from 10 to 64 Gm. The total period of observation varied from nine to 12 months.

The results of the treatment of these patients are difficult to evaluate because the symptoms before treatment were mild in character. Three said that they "felt better" after treatment, and two showed a definite gain in weight. Of the four who had complained of rectal discharge, three noted that the discharge had diminished or disappeared. Objective examination of the stricture showed no change except that tenderness was diminished in two of the five patients who complained of tenderness initially.

RESULTS OF SPECIAL STUDIES

The Complement Fixation Reaction.—The complement fixation reaction of the patients' serum was determined before treatment and at intervals afterward. A total of 104 serums were tested, or an average of 5.5 samples per patient. Most serums were tested repeatedly, so that a total of 287 tests were done.

A definite and consistent fall in the antibody titer was observed for two of the three patients with acute inguinal adenitis treated with aureomycin. One patient (G. L.) who had the most complete series of studies showed a highly significant drop in titer from 1,280 to 40.

In the group of patients with rectal lesions (tables 2 and 3) there was no significant change in the antibody titer of the serum following treatment. Only the initial and final values are presented in the tables, but the serial determinations showed no significant deviation from these. The final value is in some cases the same as the initial one, or the titer may be one dilution higher or lower. Such changes are within the limits of error of the method and are without meaning. There was no demonstrable correlation between the clinical response to treatment and the antibody titer. However, in general there was some correlation between the duration and clinical activity of the disease and the height of the antibody titer. The patients with fresh, active infections usually showed a relatively high antibody titer, while the titer was lower in the more chronic cases, such as those in which there was a long-standing stricture and a previous colostomy (table 3).

The Albumin-Globulin Ratio.—This was likewise determined before and at intervals after treatment of the patients with rectal infections. With two exceptions, all exhibited an initial hyperglobulinemia. The mean of the albumin-globulin ratio before treatment was 0.55, as compared to 0.59 at the time of the final observa-

tion. The difference is not statistically significant. However, there was a slight increase in the total serum protein concentration from a mean of 7.9 Gm. per 100 cc. before treatment to 8.6 Gm. per 100 cc. after treatment. This change has statistical significance ($P<0.05$).[10] These results differ considerably from those of Schamberg,[11] who found an appreciable decrease in the concentration of serum globulin following the treatment of 20 patients with lymphogranuloma buboes with sulfanilamide.

Biopsy of the rectal mucosa of 10 patients with rectal strictures or proctitis showed nonspecific proctitis or granuloma of the rectum. The histological appearance was considered to be entirely compatible with lymphogranuloma venereum but not diagnostic of it. Isolation of the virus from the biopsy material from three patients was attempted without success. Failure may have been due to the smallness of the fragments of tissue submitted for study, since others[12] have isolated the virus from rectal strictures. Liver biopsy in five cases revealed no histological change, and attempts to isolate the virus from this tissue likewise gave negative results.

COMMENT

Clinically, our results are similar to those of Wright and his associates.[7] All the patients with buboes showed an excellent response to treatment, and seven of the nine with proctitis or early rectal strictures were improved. In two of these patients, however, the improvement was only temporary. It is difficult to understand why symptomatic improvement is so definite and so lasting in some cases in which there is little objective change in the stricture. Possibly there is some relief of spasm due to tenderness at the site of stricture. In the natural course of the disease most, if not all, of these patients would eventually require colostomy because of increasing obstruction. So far, two of our nine early patients have required a colostomy. Both of these had advanced strictures when treatment was started. It is, of course, unreasonable to hope that aureomycin can cure a thick, fibrous stricture with a lumen sufficiently narrowed to cause signs of partial obstruction. It is more important to ask what will happen to the other seven patients. A final answer can be obtained only by years of observation. It is possible that aureomycin may save some of these patients from colostomy by destroying the virus and thus interrupting the process of continued infection and fibrosis which leads eventually to obstruction.

On the other hand, our observations, as discussed below, would indicate that some of the viruses may survive, even after a month of treatment with aureomycin. If this is so, one would expect in time to see continued evidence of infection and progressive narrowing of the stricture in spite of treatment. Possibly these patients will require treatment with aureomycin over a period of many months. It seems clear, therefore, that the field of greatest usefulness of aureomycin in the

10. Fisher, R. A.: Statistical Methods for Research Workers, London, Oliver & Boyd, Ltd., 1938. Francis, T., Jr.: Mechanisms of Infection and Immunity in Virus Diseases of Man, Bact. Rev. **11**:147-156, 1947.

11. Schamberg, I. L.: The Course of the Plasma Protein Changes in Early Lymphopathia Venereum Under Treatment with Sulfanilamide, Am. J. M. Sc. **201**:67-81, 1941.

12. Palmer, W. L.; Kirsner, J. B., and Rodaniche, E. C.: Studies on Lymphogranuloma Venereum Infection of the Rectum, J. A. M. A. **118**:517-524 (Feb. 14) 1942.

treatment of lymphogranuloma venereum is in those patients with acute inguinal adenitis, with proctitis or with early rectal strictures. In patients in whom a colostomy is required aureomycin may still be of value in treating the persistent rectal infection. One may thus hope to avoid the troublesome sequelae of chronic infection which have led some surgeons to advise resection of the rectum in order to restore the patient to health.[13] On the other hand, preliminary treatment with aureomycin may add to the safety of surgical procedures. Wright and his associates have suggested [14] resection of an obstructing stricture, after preliminary colostomy, with eventual restoration of the continuity of the bowel. In the past we have avoided such procedures because of the technical difficulties due to active infection and because of the probability of recurrent disease of the bowel after resection. However, with the aid of aureomycin, operations of this type might be indicated in selected cases.

Although we must conclude on the basis of clinical observations that aureomycin has some value in the treatment of lymphogranuloma venereum, it is important to determine, if possible, whether the infecting virus is eliminated by oral treatment or whether it may persist in the host in a latent form (which may be the agent of chronic, progressive disease). It has been demonstrated experimentally [15] and in human infections [12] that the virus may persist for long intervals following infection. Jones, Rake and Stearns [16] demonstrated that 30 per cent of mice surviving after lymphogranuloma infections treated with sulfanilamide became carriers of the virus. It seems clear that favorable clinical results in the treatment of lymphogranuloma infections are not necessarily accompanied with eradication of the virus. The complement fixation test with the lygranum antigen measures the concentration of complement-fixing antibodies to the agents of the psittacosis-lymphogranuloma group. A positive reaction is considered indirect evidence of past or present infection. The test does not clearly differentiate, however, between active and latent infections, but since the lymphogranuloma virus is known to persist in certain hosts for long periods one may assume that a positive reaction to the test, especially when in high titer, signifies the presence of the virus. The infection may be clinically latent, as was one of the laboratory infections described by Harrop, Rake and Shaffer.[17] However, the absence of antibodies does not necessarily prove the absence of the virus, as shown by Wall [18] in experimental

13. Bacon, H. E.: The Surgical Treatment of Lymphogranulomatous Stricture of the Rectum, South. M. J. **34**:31-35, 1941. Barber, W. H., and Murphy, W. B.: Lymphogranuloma Venereum, Ann. Surg. **113**:30-40, 1941. Runyan, J. W.; Kraft, L. M., and Jorden, I.: Effect of Aureomycin on the Survival of Virus in Lymphogranulomatous Buboes, Am. J. Med. **7**:419-420, 1949.

14. Wright, L. T.; Berg, B. N.; Bolden, J. V., and Freeman, W. A.: Rectal Stricture Due to Lymphogranuloma Venereum, with Especial Reference to Pauchet's Excision Operation, Surg., Gynec. & Obst. **82**:449-462, 1946.

15. Levaditi, C.: Particularités de l'infection lymphogranulomateuse de la souris, Compt. rend. Soc. de biol. **138**:749, 1944.

16. Jones, H.; Rake, G., and Stearns, B.: Studies on Lymphogranuloma Venereum: III. The Action of the Sulfonamides on the Agent of Lymphogranuloma Venereum, J. Infect. Dis. **76**:55-69, 1945.

17. Harrop, G. A.; Rake, G. W., and Shaffer, M. F.: New Clinical Conceptions of Lymphogranuloma Venereum, Tr. A. Am. Physicians **56**:101-105, 1941.

18. Wall, M. J.: Complement-Fixing Antibodies of Lymphogranuloma Venereum in Mice: Their Development and Response to Sulfonamide Therapy, J. Immunol. **55**:353-361, 1947.

infections of mice treated with sulfanilamide. In some animals the antibodies disappeared but the virus could still be recovered, although with some difficulty.

In the treatment of human infections with the sulfonamides, complement-fixing antibodies persisted in spite of a good clinical response.[19] These observations would suggest the persistence of the virus in spite of treatment, and in fact Heyman, Wall and Beeson[20] report the isolation of the virus from an excised lymph node six months after the onset of symptoms and four months after treatment with 120 Gm. of sulfathiazole.

In our experience two cases of acute adenitis were the only ones in which a pronounced fall in the antibody titer was noted after treatment. It seems probable that the virus was completely eliminated in these early, acute infections, but the patients will have to be followed to determine whether or not this is true. In this connection it should be stated that in two patients with adenitis treated orally with 24.5 Gm. (nine days) and 19.5 Gm. (10 days) respectively, virus could be isolated on the first and second days of treatment but not after four to seven days. One is not certain whether the virus was entirely eliminated or merely reduced in quantity so as to be no longer detectable on the fourth to seventh days of treatment.[11] In a consideration of the results in the more chronic group of infections with rectal lesions, there are two possible explanations for the clinical improvement which was noted without a decline in antibody titer: (1) the virus was eliminated by aureomycin treatment but there was a delay in the fall in the antibody titer or (2) some virus particles were destroyed, as indicated by clinical improvement, but some persisted in a latent form. The first possibility seems unlikely in view of the prompt fall in the antibody titer observed in the cases of adenitis. In considering the second possibility, one is tempted to speculate on the possible role of the extracellular phase in the development of agents of the psittacosis-lymphogranuloma group described by Weiss.[21] Others[22] have suggested a possible association between the existence of an extracellular phase in the development of these agents and their susceptibility to sulfonamides or antibiotics. Thus one may conjecture that in early acute lymphogranuloma infections, when most of the virus is actively multiplying (going through the extracellular as well as the intracellular phase), aureomycin would be most effective, whereas in patients with rectal strictures of long standing all the virus may exist as intracellular virus and aureomycin may be entirely ineffective. In the patients with progressive rectal lesions (proctitis and early stricture) the actively multiplying virus may be eliminated by aureomycin, with resulting clinical improvement, but some latent viruses may survive and complement-fixing antibodies may therefore persist.

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19. Grace, A. W., and Rake, G.: Complement Fixation Test for Lymphogranuloma Venereum: Results Obtained with Its Use, Arch. Dermat. & Syph. **48**:619-625 (Dec.) 1943. Harrop and others.[17]

20. Heyman, A.; Wall, M. J., and Beeson, P. B.: The Effect of Sulfonamide Therapy on the Persistence of the Virus of Lymphogranuloma in Buboes, Am. J. Syph., Gonor. & Ven. Dis. **31**:81-86, 1947.

21. Weiss, E.: The Extracellular Development of Agents of the Psittacosis-Lymphogranuloma Group (Chlamydozoaceae), J. Infect. Dis. **84**:125-149, 1949.

22. Eaton, M. D.; Dozois, T. F.; Van Allen, A.; Parish, V. L., and Schwalm, S.: Studies on Inhibition of the Agents of Murine and Feline Pneumonitis by Penicillin, J. Immunol. **58**: 251-267, 1948. Fisher.[10] Jones and others.[16]

SUMMARY

Nineteen patients infected by the lymphogranuloma venereum virus, including three with inguinal adenitis, two with proctitis and 14 with rectal stricture, have been treated with aureomycin, chiefly by the oral route in a total dosage ranging from 28 to 70 Gm. and have been followed for periods up to one year.

The patients with acute inguinal adenitis and those with comparatively early rectal infections showed an encouraging clinical response to aureomycin therapy, but the response of the patients with more chronic forms of the disease was equivocal.

The complement fixation test showed a definite fall in the antibody titer following treatment in only two patients with acute inguinal adenitis. The lack of a definite fall in the other 17 patients suggests the survival of virus following treatment in the more chronic infections.

The final conclusions concerning the effect of aureomycin on the course of lymphogranuloma, on the survival of the virus in the host and on the serologic pattern must await further observation of these patients over a period of several years.

ANESTHESIA FOR INFANTS AND CHILDREN

The Nonrebreathing Technic

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WITH the development of anesthesiology as a specialty have come many advances both in the pharmacologic sphere and in technics of administration of agents. In pediatric anesthesia, improvements in technic have been slower to appear, possibly because the familiar "open drop ether" method over many years apparently has satisfied the demands of both surgeon and anesthetist. Recently, however, the scope of pediatric surgery has broadened and the trained anesthetist has realized certain limitations inherent in the open drop method. Now many infants enter the hospital for surgery about the head and neck, and for these the anesthetist must shift his position from the head of the table to make room for the surgeon.

Thoracic operations in early childhood are frequent, and some method must be employed which facilitates intermittent positive pressure and provides adequate oxygen. The necessity of an absolutely patent airway is receiving increasing thought among those who are aware of how easily only a partial obstruction over a period of time will decrease the oxygen saturation of the blood and increase the tendency to respiratory acidosis.

The presence of an ether mask on the child's face is tantamount to increasing the dead space in the circuit. It establishes a cycle in which the percentage of oxygen gradually falls, while that of carbon dioxide increases in the inhaled mixture.[1] Such factors are instrumental in altering the metabolic equilibrium of the patient.

From the pharmacologic aspect, ethyl ether has withstood the test of time because of its wide margin of safety, its actual stimulant effect on respiration in operable planes of anesthesia and its ease of administration. These are all points of great importance when one considers the narrow margin of safety which exists in children, but when ether is used as the only agent to produce anesthesia, metabolic disturbances result. Liver function is impaired, glycogenolysis is increased, the blood sugar and blood cholesterol levels are elevated, hemoconcentration appears, excessive production of lactic acid tends toward a metabolic acidosis and kidney function diminishes. When these factors are added to the upsets occasioned

From the Department of Anaesthesia, Children's Memorial Hospital, and McGill University.

1. Faulconer, A., Jr., and Latterell, K. E.: Tensions of Oxygen and Ether Vapor During Use of the Semi-Open, Air-Ether Method of Anesthesia, Anesthesiology **10**:247-259, 1949.

by the operation itself, one wonders if perhaps some other agent or combination would be of more benefit to the patient.

In adults there has been a marked trend toward "balanced anesthesia," in which small amounts of several agents may be utilized to provide satisfactory conditions for the surgeon. No agent is used to excess, and as a result physiological disturbances are seen less frequently.

A similar "balanced anesthesia" would seem advantageous for children. This anesthesia is possible only when gas machines are employed. Those in use at present possess such resistance to respiration that children under 6 years of age become fatigued easily. In addition, it is difficult to eliminate dead space to the extent that carbon dioxide does not accumulate gradually. It is most distressing to see a child who has been subjected to anesthesia for an hour by means of a closed circle absorption technic. The pulse is rapid, blood pressure is mounting, the patient is perspiring and respiration is rapid and performed with considerable effort. Anesthesia may be disturbing the patient's physiology more than the surgical intervention.

With these facts in mind, the problem presented is to evolve a technic in which a certain freedom of action is given to the surgeon and the anesthetist, respirations may be easily assisted or controlled and a patent airway is assured though the anesthetist may be away from the head of the patient. Such a system should reduce dead space so that even the tiniest infant may be safely anesthetized. There should be no opportunity for carbon dioxide to accumulate, and resistance to respiration should be minimal. Finally, it should be possible to employ a combination of agents without inconvenience.

NONREBREATHING VALVE

Several years ago, Leigh [2] met a number of these requisites when he introduced a nonrebreathing valve, which a little later was modified to some extent.[3] Since 1947 this valve has been in daily use at the Children's Memorial Hospital and has proved satisfactory in all types of cases. The simplicity of design of the valve has been advantageous. The less complex a mechanism is, the fewer are the difficulties encountered with it. Figure 1 shows the essential parts of the apparatus. In the supporting light metal framework two rubber disks are placed in such a way that the gases inhaled can come only from the source of supply, while the exhalations are blown off into the atmosphere. Each valve disk is held in place and attached to its seat by a small central prolongation. The mechanical efficiency of this arrangement is of a high order. The rubber disks possess such inherent resiliency that they lie naturally in close contact with their seats, and yet they are so light that they offer little resistance to opening. At each end of the metal frame are two nipples. To the nipple which is set within the rubber cork is attached a 2.5 liter reservoir bag. When the rubber cork is detached, one may reach with a pair of forceps into the frame and remove the valve disk inside for cleaning purposes. In older children or adults, for whom a larger reservoir is required, it

2. Leigh, M. D., and Kester, H. A.: Endotracheal Anesthesia for Operations on Cleft Lip and Cleft Palate, Anesthesiology **9**:32-41, 1948.

3. Stephen, C. R., and Slater, H. M.: A Nonresisting, Nonrebreathing Valve, Anesthesiology **9**:550-552, 1948.

is found that the neck of a 5 liter bag will fit snugly over the metal frame. Over the nipple at the other end of the frame is slipped a short piece of rubber tubing to which various sizes of endotracheal connectors may be attached.

The rubber valve disks preserve their efficiency and resiliency for 12 to 18 months with constant usage. In normal circumstances water vapor from the patient's exhalations does not condense on them, and thus they do not become sticky or lose their efficiency. If the valve flaps happen to become contaminated by vomitus, they may be washed with soap and water and cleaned with ether without harm. The rubber parts will not withstand boiling or autoclaving, and these measures have not been found necessary. Placing a little talcum powder on the rubber disks from time to time appears to aid in preserving their life.

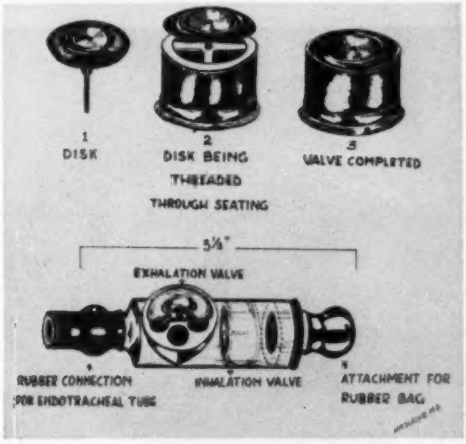

Fig. 1.—Component parts of nonrebreathing bag.

ADVANTAGES

Figure 2 shows the valve in use. The technic is described as orotracheal nonrebreathing. Gases flow from the anesthetic machine into the reservoir bag. The inspiratory effort of the patient opens the valve within the frame and the anesthetic mixture passes into the lungs. During exhalation the valve to the bag is closed and the gases pass off into the atmosphere as the other valve opens.

The resistance encountered by the patient in lifting the rubber disks is small. At a flow rate of 15 liters per minute, which is about the highest encountered in children, the resistance to inhalation is 1.75 cm. of water and that to exhalation is 1.0 cm. of water.[4] In smaller children, in whom the flow rate is less, the resistance would not be as high.

The dead space in such a technic is reduced to a minimum. The presence of the endotracheal tube reduces the rebreathing content of the mouth considerably, and the dead space in the valve proper is 10 cc. Even in the smallest infants

4. Courtesy of Dr. William Neff.

accumulation of carbon dioxide has not been a problem in such circumstances. The fact that there is no rebreathing from the reservoir bag is added protection against the development of a gaseous acidosis.

Assisted and controlled respirations may be carried out in this technic with ease and exactitude. Even though the surgeon may be working in the head region, there need be no interference with the operative procedure. By placing a finger over the exhalation valve during the inspiratory phase and simultaneously squeezing the reservoir bag with the other hand, any degree of assistance to inspiration may be given to the patient. During exhalation the finger is removed from the exhalation valve and the bag allowed to refill with the mixture from the machine. Many anesthetists can gage the amount of positive pressure by the feel of the reservoir bag, or this may be recorded accurately by including a water manometer

Fig. 2.—Position of nonrebreathing valve between endotracheal tube and reservoir bag.

in the circuit between the gas machine and the reservoir bag. The presence of the bag close to the patient's head is a technical advantage to the anesthetist.

Since there is no rebreathing with this method, the flow of gases from the anesthetic machine must be at least equal to the patient's minute volume. It is suggested that the rate of flow be adjusted so that the reservoir bag is kept moderately full but not distended. In a child of 6 or 7 years it is usual to begin with a flow of 6 liters of nitrous oxide and 2 liters of oxygen per minute. This 75:25 ratio provides sufficient oxygen for the patient, and because there is no rebreathing the ratio will remain the same.[5] The rate of flow of the gases may be altered as the situation demands.

5. Crowley, J. H.; Faulconer, A., Jr., and Lundy, J. S.: Certain Factors Influencing the Percentage of Oxygen in Mixtures of Nitrous Oxide and Oxygen, Anesth. & Analg. **27**:256-261, 1948.

REVIEW OF CASES

In the last 18 months 2,026 infants and children have been anesthetized according to this technic. All age groups have been included, as can be seen in table 1. In infants a few days old undergoing major procedures the endotracheal nonrebreathing method is employed by preference.

The types of operative procedures have been varied (table 2). Although by surgical standards a tonsillectomy may be considered a minor procedure, it has not been treated as such from the anesthetic aspect. It is in this type of operation that the orotracheal nonrebreathing technic has proved of greatest value. The anesthetist is out of the way of the surgeon, there need be no fear of aspiration

TABLE 1.—*Age of Patients*

Years	—1	—2	—5	—10	+10	
Cases	191	203	656	795	179	Total, 2,026

TABLE 2.—*Surgical Procedures*

Ear, Nose and Throat	Intra-Abdominal		Plastic	Head and Neck (Other Than Plastic)		Genitourinary
1,073	306		294	116		71
	Trunk	Orthopedic		Extremities	Thoracic	
	50	48		40	28	

TABLE 3.—*Duration of Procedure (Hours)*

—½	—1	—2	+2
334	996	522	174

TABLE 4.—*Anesthetic Agents*

Vinethene,® Ether and Nitrous Oxide	Thiopental Sodium, Nitrous Oxide, Curare	Kemithal, Nitrous Oxide, Curare	Thiopental Sodium, Curare, Nitrous Oxide, Trichlorethylene
1,773	175	36	42

of blood or detritus, a patent airway is assured at all times and the patient may be maintained in an even, moderately light plane of anesthesia.

The duration of anesthesia is shown in table 3. The commonest agents of induction employed were vinyl ether (vinethene®) followed by ether, with the use of the open drop mask or thiopental sodium–curare intravenously. With both these methods induction was rapid, and delays were not caused by insertion of the endotracheal tube.

The anesthetic agents employed are shown in table 4. The most frequent combination used for maintenance was nitrous oxide and ether. It is remarkable how little ether was required when nitrous oxide and oxygen in a 75:25 ratio were used as gaseous vehicles. The presence of the endotracheal tube allowed the anesthetist to carry the patient in light planes of narcosis, because he did not need to worry about the possibility of reflex spasm of the vocal cords. Moreover,

with the tube in place, adequate relaxation could be obtained in lighter planes. In these circumstances the amount of ether required for most procedures was not considered sufficient to cause metabolic disturbances.

The only limitations to the employment of the barbiturates and muscle relaxants were the skill of the anesthetist and the inability to get into a vein in smaller children. It was recognized that these agents produced depression of the respiratory mechanisms and were not safe in the hands of beginners or untrained residents.

CASE RECORDS

Figure 3 shows the anesthetic record of a 14 month old boy weighing 20 pounds (9 Kg.) during a pulmonary-subclavian anastomosis for tetralogy of Fallot. The hemoglobin content was 16.5 Gm. per 100 cc. Induction was by means of open drop vinethene® and ether. A no. 2 B portex (vinyl plastic) endotracheal tube was employed and anesthesia maintained with nitrous oxide, oxygen, small amounts

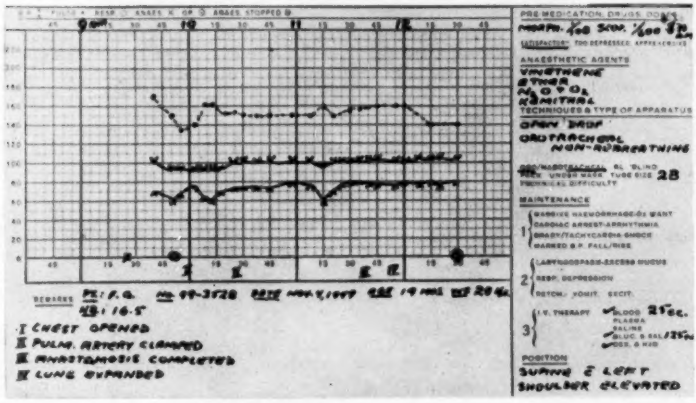

Fig. 3.—Anesthetic record of infant undergoing operation for tetralogy of Fallot (duration, 3 hours).

of ether and kemithal sodium (5, cyclohexamyl-5-allyl-2-thiobarbituric acid). The extremely short-acting barbiturate was given in small doses of 1 to 2 cc. intermittently to reduce the amount of ether required and hence lessen the danger of increasing the hemoconcentration. Procaine, 0.2 per cent, was run as a slow continuous drip with 5 per cent glucose and saline. Respirations were assisted throughout the greater part of the procedure.

Figure 4 is a record of a 3 month old girl weighing 10.5 pounds (4.7 Kg.) who was operated on for excision of a large hemangioma in the parotid region. Induction was with open drop ether, and a no. 0 portex tube was employed for intubation. Maintenance was with nitrous oxide and oxygen in a 70:30 ratio, with small amounts of ether added as required. After almost four hours of anesthesia, there was no increase in the respiratory rate, the blood pressure and pulse had remained steady and the patient did not appear fatigued. No sweating had occurred during operation. The baby awoke while still on the table.

The next anesthetic chart (fig. 5) is that of a toxic, dehydrated boy of 6 years weighing 42 pounds (19 Kg.) who had an "acute abdomen." Induction was with thiopental sodium and curare, oral intubation with a no. 26 tube, and maintenance with nitrous oxide and oxygen in a 75:25 ratio, along with added barbiturate and

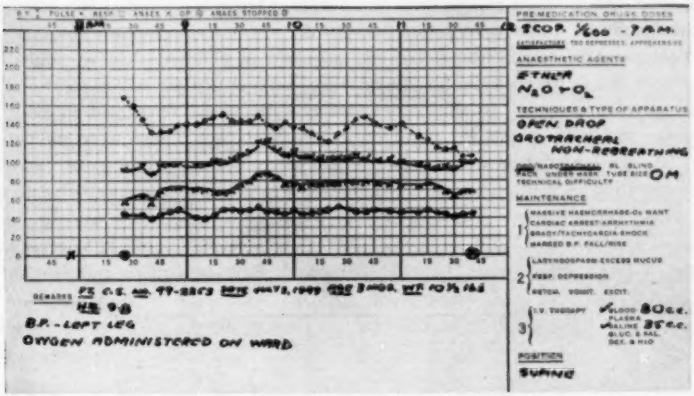

Fig. 4.—Anesthetic record of infant undergoing operation for hemangioma (duration, 3 hours and 45 minutes).

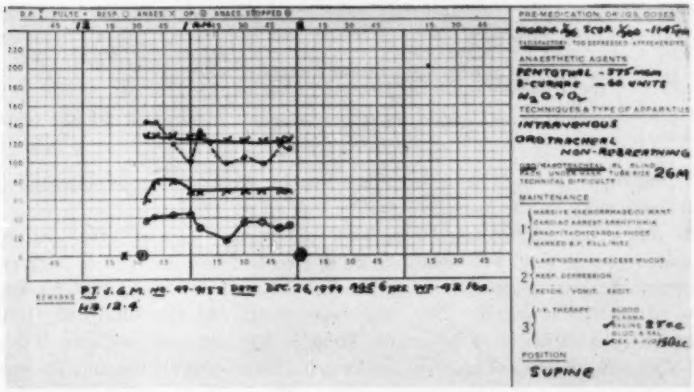

Fig. 5.—Anesthetic record of boy undergoing laparotomy and appendectomy (duration, 1 hour and 30 minutes).

curare. The gradual fall of the pulse rate and the slowing of the respiratory rate during operation were reassuring to the anesthetist.

Figure 6 is the anesthetic record of a 2½ year old boy weighing 21 pounds (9.5 Kg.) who came to the operating room extremely ill and suffering from an acute intestinal obstruction, associated with severe abdominal distention. Induction was with open drop vinethene® and ether and intubation with a no. 2 B portex

tube. Just before intubation a convulsion began in the face and rapidly spread to the arms and legs. This was thought to be due to the summation of a number of factors and was quickly controlled with intravenous administration of kemithal. The surgeon continued with a bowel resection and anastomosis, while the patient was maintained for 4½ hours on nitrous oxide and oxygen in a 70:30 ratio, along with intermittent doses of kemithal and curare. He was awake at the conclusion of the operation, and recovery was uneventful.

Postoperative complications are less common in children than in adults. In large part this is believed due to the early and intense activity which most children show after operation. In this series bronchopneumonia developed in only two children, and both responded rapidly to chemotherapy. There were no patients with laryngeal edema or with trauma to the cords who gave any cause for alarm after operation. On the table, careful attention was given by the anesthetist to fluid and blood replacement. The aim was to treat shock expectantly and to replace blood as it was lost. With the combination of nitrous oxide and light ether anesthesia, a large majority of patients recovered their protective reflexes on the

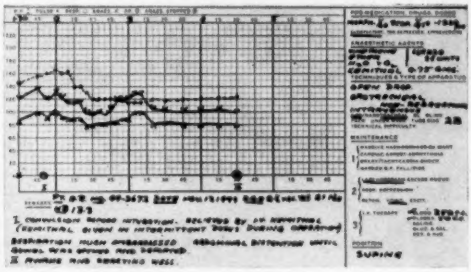

Fig. 6.—Anesthetic record of boy subjected to operation for obstruction of bowel (duration, 4½ hours).

operating room table. This is considered to be a mark of good anesthesia and contributes much to the low postoperative morbidity.

In this series of 2,026 cases there were four deaths. One of these occurred 11 days after operation in a 3 month old child who had been brought to surgery for reduction of a strangulated hernia. At the postmortem examination no definite cause of death was found. The lungs were clear. Another death occurred 72 hours after operation, in a premature baby 3 days old and weighing 5 pounds (2.3 Kg.) who underwent anastomosis for a tracheoesophageal fistula. The patient appeared to stand the operation moderately well and died suddenly. At autopsy the lungs and heart were normal.

The other two fatalities occurred in the operating room. One was due to a massive uncontrollable hemorrhage in a 20 month old infant. The second was in a 3 month old baby weighing 10 pounds (4.5 Kg.) who was undergoing an excision of a large lymphangioma involving the right hand and forearm. In this infant anesthesia was induced with open drop ether, intubation was done with a no. 0 portex plastic tube and nitrous oxide and oxygen in a 70:30 ratio was used for maintenance of anesthesia, with small amounts of ether added from time to time.

A tourniquet was on the arm. The baby did well for 1½ hours, with the pulse remaining steady at a rate of about 120 per minute and the respiratory rate ranging between 50 and 60 per minute, not unduly rapid for an infant of this size. Suddenly the pulse rate began to increase rapidly, and then the heart stopped. Cardiac massage was instituted immediately but to no avail. At autopsy no cause for death was found. It is felt that this must be considered an anesthetic death, the only one in the series.

COMMENT

The orotracheal nonrebreathing technic is believed to possess definite advantages for the patient, surgeon and anesthetist. The method is physiologically sound and produces a minimal disturbance of the patient's metabolism. It is sufficiently self regulatory so that the anesthetist can be free to adjust intravenous flows, take blood pressures and keep records. This is frequently not the case with other technics used in children. Objections may be raised regarding the necessity of employing endotracheal tubes. In the series reviewed here, there have been no serious complications resulting from their utilization. A number of children have had hoarse cries for several hours, but none have shown sufficient obstruction of the upper respiratory tract to give cause for alarm. In pediatric anesthesia, it is certain that the advantages of intubation far outweigh the disadvantages.

SUMMARY

A description is given of the nonrebreathing valve. The advantages of the orotracheal nonrebreathing technic in pediatric anesthesia are presented. A series of 2,026 cases involving infants and children are reviewed, with illustrative case records.

AMEBIC ABSCESS OF THE LIVER—THERAPEUTIC APPROACHES

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WHEN one searches for a plan of therapy for amebic abscess of the liver in 1950, the adjunctive use of antibiotics is expected to be in that plan. Leonard Rogers[1] (1922) actually formulated the basis of modern therapy by proving that Endamoeba histolytica was the etiological agent and that emetine was specific for the disease. He reduced the mortality rate from 57 to 14 per cent by the introduction of emetine as the antiamebic and of the more conservative closed aspiration drainage instead of open drainage, which prior to this time had been associated with dangerous sequelae.

The excellent 1943 monograph by Ochsner and DeBakey[2] remains the actual guide, although their plans were largely concerned with surgery and antiamebics and not with antibiotics. Sporadic reports concerning the adjunctive role of the use of antibiotics with promising results have recently appeared.[3] It may be superfluous to add that antibiotics should accompany any plan of therapy because the accompanying secondary pyogenic infection is well known and it is logical to believe that control or partial control should be obtained by their use. The low mortality rate (3.5 per cent) reported by Ochsner and DeBakey was hardly expected to be further lowered, although one recognizes from their report that there were many heroic last minute attempts to save the patient in some of their desperate cases. We believe that the mortality can be lowered to about 1 per cent or less with the use of the proper drugs and conservative surgical intervention, and we include in this report comments on the treatment used in 16 consecutive cases in which no fatalities occurred. Several of the desperate cases are briefly outlined to illustrate points which to us are of paramount importance in the progressive steps one takes to bring about cure or control.

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Rogers, L.: Amebic Liver Abscess: Its Pathology, Prevention, and Cure: Lecture I. Etiology and Pathology of Amebic Liver Abscess, Lancet **1**:463-469, 1922; Lecture II. The Varieties and Treatment of Amebic Liver Abscess, ibid. **1**:569-575, 1922; Lecture III. The Prevention of Amebic Liver Abscess and the Recent Reduction in Its Prevalence and Mortality, ibid. **1**:677-684, 1922.

2. Ochsner, A., and DeBakey, M.: Amebic Hepatitis and Hepatic Abscess: Analysis of 181 Cases with Review of Literature, Surgery **13**:460-493, 1943.

3. Ferguson, L. K., and Anderson, R. K.: Amebic Liver Abscess in Service Personnel, Gastroenterology **8**:332-342, 1947.

Some important points should be mentioned because no therapy for amebic liver abscess can be rationally accomplished without a knowledge of them.

1. An awareness of the possibility of the disease must be present in the minds of the physicians or surgeons who study the case, or lengthy dangerous delay in introduction of therapy will follow.

2. Pathogenicity and epidemiology of the disease are not accurately established. The disease is not always of tropical or subtropical distribution,[4] and a single member of a family may demonstrate clinical amebic disease while the other exposed members do not or may never demonstrate it.

3. Certain pathological facts must be known: (*a*) Liver abscess appears in 4 to 17 per cent of cases of intestinal amebiasis.[5] At Kennedy Hospital there were 16 cases of proved liver abscess in 163 cases of amebiasis, an incidence of 9.8 per cent. It predominates in males (90 to 95 per cent). (*b*) Amebic hepatitis antedates amebic abscess and is produced by the introduction of the amebas into the liver via portal tributaries.[6] The abscesses are usually single and located in the right lobe of the liver (96.3 per cent).[2] They may perforate and enter the subhepatic and subphrenic spaces, pleura, bronchus, lung, pericardium, lumbar region, stomach, colon, vena cava, kidney, bile ducts and duodenum.[4a] It is believed that bloodstream amebic infections (brain, kidney) are more frequently noted when liver abscess is present.[7] (*c*) The pus is of typical appearance, termed "chocolate sauce," "anchovy paste," "wine dreg" and "salmon pink." (*d*) Secondary pyogenic infection is common (50 per cent incidence, Strong[8]). (*e*) Amebas are not found in pus as commonly as one would expect (incidences of 16.5 per cent[2] and 65 per cent[4a] are reported). In our cases, two in seven uncomplicated abscesses contained the organism. In the pleuropulmonary cases, amebas were found in the sputum in three and in empyema drainage in one.

4. There are systemic and local symptoms. The systemic symptoms are fever, weakness, weight loss, chills, sweats, diarrhea, nausea and vomiting, and jaundice. Jaundice is least common of all; it was present in one of our cases. A history of diarrhea may be absent, but if present it usually precedes the symptoms of liver abscess by one to three months. The incidence of diarrhea reported ranges from 45 to 85 per cent.[9]

The local symptoms are pain and tenderness over the liver (95 per cent of cases) and hepatomegaly (75 per cent). Pain in the right shoulder is common.

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4. (*a*) Craig, C. F.: The Etiology, Diagnosis, and Treatment of Amebiasis, Baltimore, Williams & Wilkins Company, 1945. (*b*) Bulletin 50, Article 376, War Office, British Army Medical Department, 1945. (*c*) Ochsner and DeBakey.[2]

5. Ochsner and DeBakey.[2] Craig.[4a]

6. Rogers.[1] Ochsner and DeBakey.[2] Ferguson and Anderson.[3] Craig.[4a]

7. Halpert, B., and Ashley, J. D., Jr.: Amebic Colitis Complicated with Abscess of the Brain, Arch. Path. **38**:112-114 (Aug.) 1944.

8. Stitt, E. R.: Stitt's Diagnosis, Prevention, and Treatment of Tropical Diseases, edited by R. P. Strong, ed. 6, Philadelphia, The Blakiston Company, 1942, vol. 1.

9. (*a*) DeSilva, S.: Significant Observations on Amebic Hepatitis: Clinical Review of 200 Patients, J. Trop. Med. **48**:152-157, 1946. (*b*) Galloway, B. T.: Extra-Intestinal Amebiasis and Its Diagnosis, New Orleans M. & S. J. **98**:373-384, 1946. (*c*) Ochsner, A.; DeBakey, M.; Kleinsasser, R., and DeBakey, E.: Amebic Hepatitis and Hepatic Abscess, Rev. Gastroenterol. **9**:438-447, 1942. (*d*) Ochsner and DeBakey.[2] (*e*) Craig.[4a]

In our cases hepatomegaly was present in eight cases and a localized mass in the epigastrium in three.

The significant laboratory findings are (1) leukocytosis (15,000 to 20,000[4a]); (2) secondary anemia; (3) a sedimentation rate markedly elevated, and (4) positive stools, present in about 50 per cent of cases [10] (43.7 per cent of our cases).

5. The complement fixation test (Army Medical School technic) is valuable if the reaction is positive and if symptoms are suggestive of hepatic abscess, in spite of normal stools. It is a sensitive test in extraintestinal forms. It elicited a positive reaction in nine of our 15 cases in which it was used (60 per cent).

6. Liver function tests are not valuable except in eliminating similar diseases. If hepatic amebic disease is of long duration, one expects decreased proteins, reversed albumin-globulin ratio and some abnormalities in thymol turbidity, sulfobromophthalein, prothrombin, serum bilirubin and cephalin flocculation, but these abnormalities are not indicative of amebic disease. Broadly, the liver function should be unaltered in early amebic infection of the liver. If there are positive reactions to the test and the disease is short lived, one would regard these as evidence against the amebic source of the suspected hepatic disease. It should be noted that malnutrition and its selective deficiency state may accompany amebic hepatic abscess (case 2) and indirectly, therefore, alter the reaction to liver function tests, but the alteration is due to the prolongation of the disease rather than to the type of organism involved.

7. The roentgenologic findings are significant. Positive diagnosis is claimed in 45 to 100 per cent of cases [11] by this method. Elevation of the diaphragm is seen, with a characteristic bulge (fig. 1 *A*) and immobility of the hemidiaphragm, usually on the right, and a reaction at the lung base, occasionally atelectatic, pleural effusion and blunting of the costophrenic sinus. With an abscess of the left lobe, there may be displacement of the barium-filled cardia and the duodenal bulb. Eleven of our cases revealed abnormalities of the right hemidiaphragm. Two of the pleuropulmonary cases may well have demonstrated these abnormalities except that the diaphragm was obscured by the pulmonary changes. Thus only one abscess of the right lobe failed to show the typical roentgen findings. In neither of the two cases in which the left lobe was involved were there diaphragmatic abnormalities, but one showed the characteristic deformity of the barium-filled stomach.

Air or opaque liquids have not been employed routinely in these cases or considered necessary. Pneumoperitoneum was performed twice without benefit diagnostically. We are in agreement with Munk [12] and with Ochsner and others [9c] that such procedures are dangerous and not essential.

8. Aspiration is used when the diagnosis is strongly suspected and if a palpable fluctuant mass presents in a site compatible with safe insertion of the needle. Simple aspiration and visual examination of pus will frequently and positively verify the diagnosis. At the time of aspiration, one should be prepared to continue the removal of the pus by this method, so that a therapeutic as well as diagnostic benefit can be obtained with one insertion of the needle.

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10. Sodeman, W. A., and Lewis, B. O.: Amebic Hepatitis: Report of 33 Cases, J. A. M. A. **129**:99-104 (Sept. 8) 1945. Ochsner and DeBakey.[2]

11. Isaac, F.: Roentgen Findings in Amebic Disease of the Liver, Radiology **45**:581-587, 1945. Ochsner and DeBakey.[2] Ochsner and others.[9c]

12. Munk, J.: X-Ray Appearances in Amebic Hepatitis, Brit. J. Radiol. **17**:48-53, 1944.

ILLUSTRATIVE CASE REPORTS

The following case reports illustrate the commoner problems.

CASE 1.—E. V., a 58 year old white man, was admitted to the surgical service of Kennedy Veterans Administration Hospital on Jan. 8, 1949, with an admission diagnosis of subphrenic abscess.

Present Illness.—He was well until noontime three days prior to his admission, when he noted onset of aching pain below both costal margins anteriorly. He took laxatives and induced vomiting but continued to experience the pain. The next day he had a shaking chill lasting two hours, after which a temperature of 104 F. developed. There was anorexia since onset. Bowel movements were normal, and there was no history of diarrhea or melena.

Past History.—The patient had had malaria for the past four years, treated with atabrine® (quinacrine hydrochloride). In October 1948 he sustained an injury to the right lumbar region as the result of an 8 foot (244 cm.) fall.

Physical Examination.—The temperature was 99.6 F., the pulse rate 100 and the respiratory rate 18. The blood pressure was 120/70. The patient was a well developed, fairly well nourished white man not acutely ill. Examination of the chest revealed tenderness to percussion over the right lower ribs but nothing else unusual. Examination of the abdomen and rectum revealed no abnormalities.

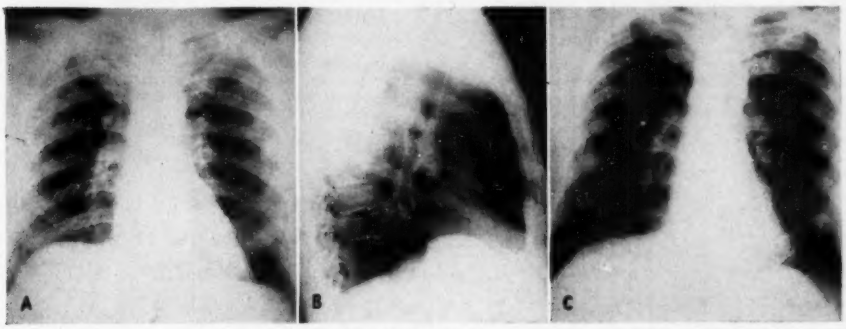

Fig. 1 (case 1).—*A*, roentgenogram of chest before treatment, showing characteristic doming of the right hemidiaphragm. *B*, lateral view of the chest before treatment, showing obliteration of the anterior costophrenic sinus. *C*, view of the chest after treatment with emetine and penicillin.

Laboratory Findings.—The red blood cell count was 4,650,000, with a hemoglobin content of 14.4 Gm., and the white blood cell count 15,200, with 89 per cent neutrophils. Urinalysis showed albumin (1 plus), occasional red cells and several granular casts. A malaria smear was negative. The prothrombin time was 100. Agglutination tests for typhoid, paratyphoid, tularemia, typhus and brucellosis gave negative reactions, as did the complement fixation test for amebiasis and the serologic test. The sedimentation rate was 30 mm. Stools did not contain parasites, and a blood culture was sterile.

Roentgenologic Findings.—A roentgenogram of the abdomen in the upright position was normal. In the chest there was doming of the right side of the diaphragm, with the anterior costophrenic sinus obliterated (fig. 1 *A, B*).

Hospital Course.—The initial impression of the examiner was that amebic hepatitis or an abscess of the right lobe of the liver was present. Penicillin was administered, but no improvement was noted. It was felt that because of the possibility of amebic hepatitis or abscess a course of emetine hydrochloride should be given. This was done, and the temperature became normal within 24 hours. With the exception of one rise to 99.6 F. on January 14, the temperature and pulse rate remained normal (fig. 2). The patient became asymptomatic. By Jan. 19, 1949, there was no elevation of the right side of the diaphragm and there was diminution of the doming

(fig. 1 *C*). Chiniofon, 0.25 Gm. three times a day, was begun on January 21 and given for 10 days. The patient was discharged on Jan. 31, 1949.

This case represents the ideal in that the patient presented himself for treatment early, while the process was still in the presuppurative or early abscess stage, which is amenable to conservative treatment. Penicillin, emetine and chiniofon were the drugs employed. It also illustrates the value of early administration of emetine. In this instance its beneficial influence was factual before a positive diagnosis of amebic liver abscess was established. Hence, control of the disease was accomplished without the aid of aspiration or of surgical exploration. Delay in the application of vigorous medical therapy could well result in chronic liver abscess, pleurobronchial extension or some of the other rarer complications.

CASE 2.—E. W., a 24 year old Negro, was admitted on Feb. 14, 1949, to the medical service, with a diagnosis of tuberculous pleural effusion.

Present Illness.—He was well until Dec. 1, 1948, when there developed swelling of the abdomen, pain in the right side of the chest, nocturnal fever, cough and dyspnea with generalized

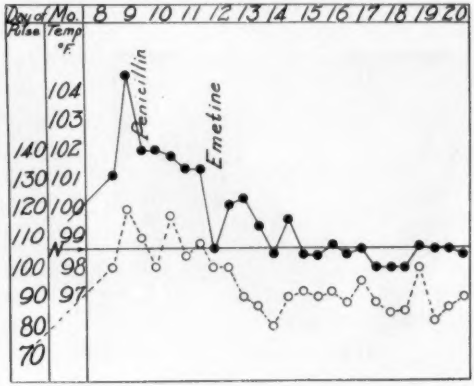

Fig. 2.—Chart showing the effect of penicillin and emetine on the temperature and pulse in case 1.

aching and headache. He was treated by a local physician with a liquid medicine, but there was little relief and the "stomach became sore." Symptoms persisted, and night sweats developed. Two weeks before his admission there was diarrhea but no melena or mucus. His appetite was good, but he could not eat because of epigastric fulness; there was nausea but no vomiting.

Past History.—The patient had been in military service in the southwest Pacific but had no illness while in the army.

Physical Examination.—The temperature was 103 F., the pulse rate 130 and the respiratory rate 36. The patient was a thin, asthenic man with a paroxysmal, dry, nonproductive cough, and he appeared acutely ill. The neck veins were slightly distended, and the trachea deviated slightly to the left. Expansion of the lungs was limited on the right, with flatness, diminished breath sounds and moist rales over the right lower region of the chest anteriorly and laterally. In the heart the point of maximal impulse was shifted to the left. The abdomen was distended. No organs or masses were palpable, and there was slight generalized tenderness, with dulness in flanks. A fluid wave was present.

Laboratory Findings.—The red blood cell count was 3,650,000, with a hemoglobin content of 10.6 Gm., and the white blood cell count 13,300, with 85 per cent polymorphonuclear cells. Urinalysis gave negative results.

Roentgenologic Findings.—There was marked elevation of the right side of the diaphragm (fig. 3 *A*).

Hospital Course.—The patient had a septic fever, with daily elevations to 103 F., and complained greatly of pain in the right lower part of the chest and the right upper quadrant. The leukocyte count increased to 16,600. Thoracenteses were attempted but were unsuccessful. The patient became worse, with increasing abdominal distention. On Feb. 21, 1949, a nonfluctuant area of induration in the right upper quadrant extending partially over the right costal margin was noted. Penicillin was administered, with a slight lowering of the temperature. On the same day an icteric tint to the scleras was noted, the serum bilirubin was 2.4 mg. and the

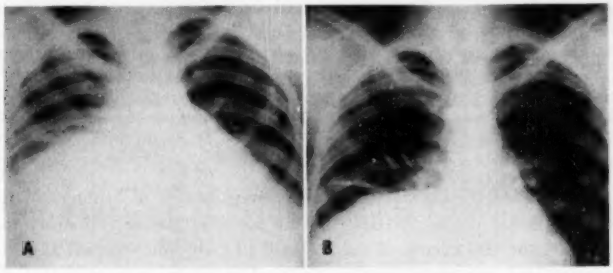

Fig. 3 (case 2).—*A*, roentgenogram of the chest before treatment, revealing tremendous elevation of the right hemidiaphragm with reaction and atelectasis in the base of the right lung. *B*, showing improvement soon after treatment with emetine, penicillin and aspiration.

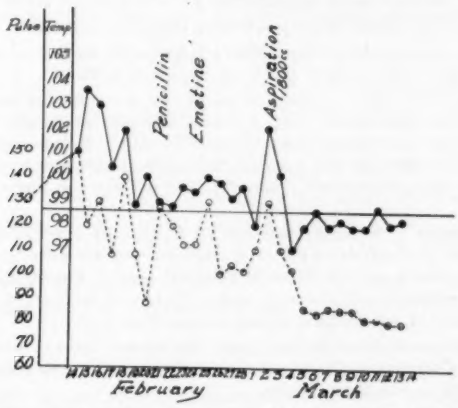

Fig. 4.—Temperature and pulse chart in case 2 showing partial response to emetine and penicillin and immediate complete response after aspiration of the liver abscess.

thymol turbidity 2.7 cc. The swelling increased, and the patient became more uncomfortable and finally irrational. He was transferred to the general surgical section, with a diagnosis of probable amebic abscess of the liver, pleurisy with effusion on the right, and pericarditis.

A complement fixation test for amebiasis on Feb. 21, 1949, was positive 1 : 32. Examination of the stools gave negative results.

Administration of emetine, 1 grain (0.06 Gm.), was begun on Feb. 24, 1949, the penicillin was increased to 200,000 units every three hours and continuous gastric suction and intravenous injections of dextrose, electrolytes, protein hydrolysate, albumin, vitamins and blood were instituted.

Two days later there was symptomatic improvement along with slight diminution in the size of the liver, but there was little change in the abdominal distention. Cephalin flocculation was 2 plus, the white blood cell count 11,750, total protein 6.2 Gm., with an albumin-globulin ratio of 0.9, and prothrombin time 38 per cent. The patient had daily bowel movements, and peristalsis was normal.

Because of the persistent abdominal distention, the possibility of tuberculous peritonitis was considered. On March 2 a paracentesis was done, and 4,360 cc. of clear straw-colored fluid was obtained from the peritoneal cavity with the characteristics of a transudate. Smears, cultures and special stains were sterile. On the same day, aspiration of the liver abscess was carried out and 1,800 cc. of "chocolate sauce" pus was obtained which proved to be negative for amebas and pyogenic organisms. Immediately after the procedure the temperature spiked to 102 F. but shortly returned to normal permanently (fig. 4).

There was notable improvement in all symptoms; the patient had a ravenous appetite, no cough and no dyspnea, the edema of the thighs and abdominal distention disappeared and the liver diminished in size. Repeated roentgenograms of the chest revealed diminution in the height of the diaphragm (fig. 3*B*). He received a course of diiodohydroxyquinoline (diodoquin®) and was discharged on April 5, 1949. A follow-up letter on March 10, 1950, stated that he was perfectly well.

Attention is called to the fact that the complex series of findings in this case are unusual in amebic disease, in spite of the fact that the early history of illness was typical. Ascites and edema of the legs are probably due to partial obstruction of the vena cava and to hypoproteinemia. Jaundice is not common in this disease.[13] After the ascitic fluid was removed the enlarged liver could easily be outlined and therapeutic drainage by aspiration was readily accomplished. Also noteworthy is the fact that only one aspiration was necessary. The severity of the patient's illness was alarming, and the favorable response was therefore dramatic.

CASE 3.—L. W., a 38 year old white man, was admitted to the medical service of this hospital on March 21, 1947, with a diagnosis of gastric ulcer, perhaps perforated.

Present Illness.—The history revealed that the patient was well until one week before his admission, when sharp, nonradiating, epigastric pain developed which was followed by fever but no chills. The pain was relieved when alkalis were taken. He vomited on one occasion, although his appetite for the most part was good. There was no history of hematemesis, jaundice, diarrhea, melena or clay-colored stools. There had been five previous similar attacks, the first one in 1930.

Physical Examination.—The temperature was 101 F., the pulse rate 120 and the respiratory rate 22. The patient was well developed, well nourished and did not seem ill. Examination showed normal lungs and heart. The blood pressure was normal. Examination of the abdomen revealed subxiphoid tenderness and moderate rigidity. There were no enlarged viscera or palpable masses. The remainder of the examination was noncontributory.

Laboratory Findings.—A complete blood count was normal; the sedimentation rate was 21 mm.; urinalysis gave negative results, as did a serologic test, and a roentgenogram of the chest on March 25 revealed no pathologic changes.

Hospital Course.—Aluminum hydroxide gel (amphojel®), an ulcer diet and a medical regimen were used for treatment. Under this program there was little improvement. On March 24 the white blood cell count had risen to 15,400, with 76 per cent polymorphonuclear cells, and by March 25 a midepigastric mass 2.5 cm. in diameter had developed which was markedly tender, firm and not fluctuant. The patient was transferred to the surgical service, and on March 26 exploratory laparotomy was done. An abscess of the left lobe of the liver was found, from which 2½ ounces (75 cc.) of salmon pink pus was obtained, which was sterile. Open drainage was instituted. Postoperatively the patient was given penicillin, gastric suction and intravenous therapy. Except for distention, which responded to suction, the convalescence was

13. Walters, W.; Watkins, C. H.; Butt, H. R., and Marshall, James M.: Amebic Abscess of the Liver Unsuspected Until Perforation, J. A. M. A. **125**:963-966 (Aug. 5) 1944.

uneventful; the temperature gradually declined, reaching normal on the eighth postoperative day (fig. 5). A complement fixation test for amebiasis gave a positive result. Stools were negative for amebas until April 11, when the organisms were first found. The patient was transferred back to the medical service on April 11 and was treated with diodoquin® and emetine. Proctoscopy and repeated examination of the stools did not reveal amebas. The patient gained 15 pounds (6.8 Kg.) and was asymptomatic two months later.

A follow-up questionnaire on March 5, 1950, revealed him to be entirely asymptomatic.

This was one of our first cases and illustrates the diagnostic difficulties encountered with abscess of the left lobe. There was lack of awareness on the part of the surgeons and physicians who first studied the patient, and accordingly duodenal ulcer was strongly suspected as a diagnosis. The diagnosis should have been definitely established at the time of exploration and emetine promptly administered.

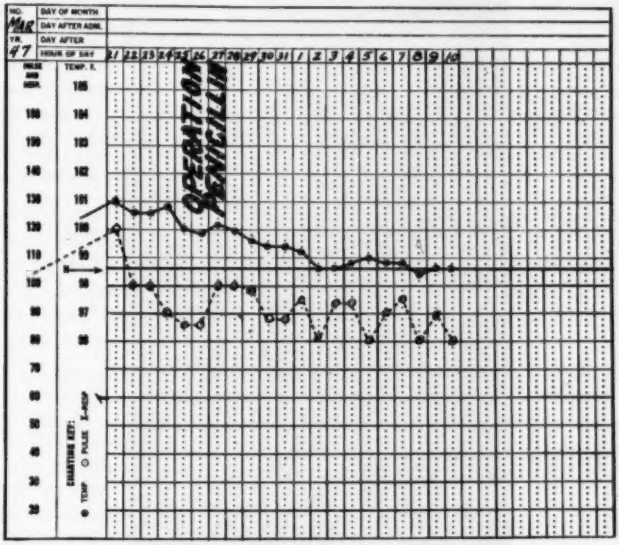

Fig. 5.—Temperature, pulse and respiration chart in case 3 showing response to open drainage and the administration of penicillin. No emetine was used in this case.

The case denotes the procrastination of the novice in regard to these two important phases. We certainly did not offer the patient the safest route to recovery.

Case 4.—H. M., a 55 year old white man, was admitted to the medical service of this hospital on Sept. 24, 1948, with a diagnosis of bronchopneumonia and carcinoma of the lung.

Present Illness.—The patient was well until one month prior to his admission, when he noted the gradual onset of fever, weakness, slight cough, night sweats and dyspnea. About two weeks later he had a severe chill, after which he was given a roentgen examination, was told he had pneumonia and received penicillin, without benefit. Hospitalization was recommended. He had lost 30 pounds (13.6 Kg.). There was no history of nausea, vomiting, abdominal pain, diarrhea or melena.

Physical Examination.—The temperature was 99.2 F., the pulse rate 100 and the respiratory rate 18. The patient was a well nourished middle-aged man who was in no apparent pain and did not appear acutely ill.

Examination of the chest revealed diminished breath sounds and fine moist rales in the lower lobe of the right lung posteriorly. The heart revealed no abnormalities, and the blood pressure was normal. Examination of the abdomen revealed no tenderness, rigidity or masses, and the liver and spleen were not palpable. The initial impression was resolving pneumonitis of the lower lobe of the right lung and possible tuberculosis.

Laboratory Findings.—The red blood cell count and the hemoglobin content were normal. The white blood cell count was 11,100, with a normal differential count. The sedimentation rate was 30 mm. Urinalysis and a serologic test for syphilis gave negative results.

Hospital Course.—Examinations of the sputum and the gastric washes for acid-fast bacilli, tuberculin tests and roentgen examination of the chest revealed nothing abnormal. The temperature rose to 102.8 F. and continued high. The patient began to complain of pain in the right lower region of the chest which was aggravated by coughing. Examination of the stools and agglutina-

Fig. 6.—Injection of the abscess cavity with iodized oil in case 4 during treatment with emetine and closed drainage.

tion tests for specific bacteria elicited negative reactions, as did skin tests for brucellosis. He became much weaker and anoretic, and the pain in the chest increased and was aggravated by coughing. The white blood cell count increased to 20,950, with 76 per cent polymorphonuclear cells. On October 23 fluoroscopy of the chest revealed limitation of movement of the right leaf of the diaphragm, with blunting of the right costophrenic sinus. A complement fixation test did not reveal the presence of amebiasis. It was felt that the patient had a liver abscess. Penicillin was administered, with slight improvement, and a 10 day course of emetine hydrochloride was started on October 26.

There was moderate improvement of the general condition and of the pain and tenderness in the right upper quadrant, but the temperature remained slightly elevated and no change was noted on roentgenograms. A few days after the course of emetine was completed the temperature rose again and dyspnea, epigastric pain and diffuse tenderness and rigidity of the upper part of the abdomen appeared. At this time there was a moderately enlarged tender liver. It was felt that

another course of emetine should be given before surgical drainage was instituted, and during this time the temperature ran a low grade, septic course. On November 18 another course of emetine was started, and again there was a response, the temperature becoming normal on the sixth day and remaining so for 10 days after the completion of the course. The liver became somewhat smaller, although roentgenograms and fluoroscopy revealed no change. On December 7 (tenth day after completion of the course of emetine) the patient had a chill followed by an elevation of the temperature to 102.6 F. It was felt that inasmuch as there was recurrence of symptoms after initial remissions and two courses of emetine surgical drainage of the abscess was indicated. Consequently, on December 9 closed drainage of the abscess by trocar was instituted through the tenth interspace into that portion of the liver sealed to the anterior chest wall. The abscess contained 250 cc. of "anchovy sauce" pus which on examination and culture revealed no pyogenic organisms. During the immediate postoperative period the patient went into shock but responded slowly to intravenous injections of albumin, blood, adrenal cortex extract (eschatin®) and phenylephrine hydrochloride (neo-synephrine hydrochloride®).

The postoperative course, otherwise, was smooth. A 14 day course of chiniofon was started on December 11. The cavity was irrigated daily with penicillin. Roentgenograms revealed progressively less elevation of the diaphragm and diminution in the size of the cavity after injection of iodized oil (fig. 6). The remainder of the course was uneventful, and the patient became asymptomatic, gained 30 pounds (13.6 Kg.) and was discharged.

Follow-up examination on May 24, 1949, revealed that the patient was healthy and asymptomatic. There was no evidence of residual or recurrent disease. Follow-up by questionnaire on March 4, 1950, revealed that there was some pain in the operative site, and he complained of arthritis in the hips which prevented his working.

This case represents an excellent response to closed drainage. However, such a measure might have been avoided and the patient possibly cured by the use of emetine hydrochloride earlier in the course. The drug was not given to the patient during the first month of hospitalization. There is every reason to believe that aspiration alone during the first or second course of emetine would have induced permanent control.

CASE 5.—W. C., a 32 year old white male farmer, was admitted to the medical service of this hospital on July 19, 1947, with a diagnosis of amebic abscess of the liver.

Present Illness.—Two months before his admission he had general malaise and fatigue and he lost 16 pounds (7.3 Kg.) in weight. Five days before admission he had diarrhea, with four to five loose watery stools without blood, fever, malaise and generalized aching which persisted for two days. There was pain in the right upper quadrant which radiated to the left upper quadrant and the right shoulder. He vomited several times in the two days prior to his admission and was treated with quinine but did not improve.

The past history revealed that he had diarrhea once while in the service in New Guinea. There were two episodes of similar pain, once in 1942 while he was on maneuvers in Louisiana and again in October 1944 while he was convalescing from shell fragment wounds in the right shoulder.

Physical Examination.—The temperature was 102 F., the pulse rate 84, the respiratory rate 24 and the blood pressure normal. The patient was undernourished and acutely ill. Examination of the heart and lungs revealed no abnormalities. The liver was greatly enlarged, exquisitely tender and soft and extended one handbreadth below the right costal margin. There was muscle guarding over the entire right upper quadrant. Digital examination of the rectum and proctoscopic examination were noncontributory. There were atrophy of the right shoulder and arm and median and ulnar nerve palsy, the result of the 1944 wound.

Initial Impression.—Liver abscess, probably due to amebiasis, was the initial diagnosis.

Laboratory Findings.—The red blood cell count was 4,550,000, the hemoglobin content 13.2 Gm., and the white blood cell count 15,000, with 83 per cent polymorphonuclear cells. A serologic test, repeated complement fixation tests for amebiasis and examinations of the stool for parasites all gave negative results. The urine was normal. The sedimentation rate was 27 mm. Amebas

were never found in the stools, in fluid from the liver abscess or the pleural cavity or in pleura removed at operation. Examinations of the sputum did not reveal any acid-fast bacilli.

On July 19, 1947, roentgenograms of the chest were normal. However, a flat plate of the abdomen revealed a moderately enlarged liver.

Hospital Course.—The patient was initially treated with emetine, penicillin and, later, sulfadiazine, without appreciable effect. Fluoroscopy of the chest on July 25 revealed almost complete immobilization of the right side of the diaphragm and some increased markings in the lower lobe of the right lung. Although the fever persisted, there was slight remission of symptoms and he had gained 2¼ pounds (1 Kg.) by August 11. On August 21 a pneumoperitoneum was performed but no abnormalities were noted.

On September 2 the symptoms became worse, and on September 5 there was onset of pleuritic pain in the right lower anterior region of the chest. Another course of emetine was given, without response. The surgical consultant felt that the patient had a liver abscess and that abdominal exploration was indicated. On September 23 an abscess of the right lobe was drained. It contained 20 cc. of chocolate brown fluid which showed no amebas or pyogenic organisms. Postoperatively, the patient was given penicillin, diodoquin® (0.75 Gm. three times a day for 10 days) and general supportive treatment. The tubes drained practically no fluid, and he continued to have a low grade fever. The abdominal wound healed without infection. On October 4 there was severe pain over the right lower part of the chest posteriorly, and on the next day there were clinical and roentgenologic signs of fluid in the chest. Thoracentesis yielded 195 cc. of thick yellow mucoid purulent material with red streaks which showed beta hemolytic Streptococcus on culture, and penicillin was given intrapleurally. The patient began to have a rather stormy course. Thoracenteses and intrapleural injections of penicillin were repeated as necessary. No amebas were ever demonstrated in the pus. Roentgenograms revealed an encapsulated empyema at the base of the right lung.

Emetine hydrochloride, 1 grain (0.06 Gm.) daily for eight days, and carbarsone, 0.25 Gm. three times a day for 10 days, were given. Within 24 hours the temperature was normal, and it remained so throughout the remainder of the hospital course. However, repeated roentgenograms of the chest revealed little change except for slight diminution in the size of the cavity. On October 25 the patient experienced light hemoptyses although his general condition was much improved. Aspirations of the chest were continued, but no improvement in the size of the empyema cavity could be seen. Consequently, on November 19, resection of the seventh right rib was done, the empyema cavity unroofed and open drainage instituted. After this the convalescence was uneventful. The wound healed by Jan. 12, 1948, and the patient was asymptomatic. Fluoroscopy revealed a small amount of pleural thickening about the area of the previously described cavity. The patient was discharged on Jan. 13, 1948.

In a follow-up letter of March 3, 1950, he stated that he felt slight pain over the liver and fulness in the abdomen but was otherwise well.

The course of events in this patient's history reveal that the proper diagnosis was made promptly and treatment with penicillin and emetine hydrochloride instituted shortly after his arrival in hospital. Ordinarily, one could expect prompt relief and perhaps permanent control. However, these did not occur, and operation with drainage failed to prevent the rupture of the abscess through the diaphragm and into the pleural cavity. Chemotherapy likewise failed to induce control even with aspiration of the chest. Finally, drainage of the empyema cavity produced the desired effect. Many courses of emetine and other antiamebics were necessary to control the disease. During abdominal operation, the abscess was observed to be small and in a high posterior position. Obviously drainage was not adequately established. Perhaps there had been partial invasion of the diaphragm at the time of laparotomy.

CASE 6.—M. W., a 26 year old white woman, was admitted to the thoracic surgery section on June 27, 1947, with a diagnosis of lung abscess and pneumonia.

Present Illness.—In the fall of 1946, during the first part of the last trimester of pregnancy, pain developed in the right upper quadrant of the abdomen, which was followed shortly by pain in the right side of the chest and a slight cough. In December 1946 she was delivered of a son by cesarean section while under gas, oxygen and ether anesthesia. Her immediate convalescence was uneventful except for anorexia, but two weeks later she became nervous, weak and easily fatigued and began to lose weight and to have a low grade fever. In March 1947 she suddenly became dyspneic, started to wheeze and coughed up large amounts of dark brown sputum which was occasionally blood streaked. Associated with this were severe pleuritic pains in the right lower part of the chest and high fever. She was hospitalized, and roentgenograms were said to show bilateral pulmonary involvement. A diagnosis of lung abscess was made. There was some improvement after treatment with penicillin and streptomycin, but one week after her discharge from the hospital the symptoms recurred, and since then she had been hospitalized almost continuously. She became progressively worse and was treated with penicillin, blood transfusions, expectorants, diathermy and oxygen, to no avail, and was finally transferred to Kennedy Hospital.

Past History.—The patient served in the army as a nurse and sustained a fracture of the right tibia in 1943, which necessitated open reduction. There was no history of tropical service or of diarrhea.

Physical Examination.—The temperature, pulse and respirations were normal. The patient coughed frequently but was in no acute distress. The chest was symmetric, but there was limitation of motion on the right, and there were diminished fremitus, dulness and absent breath sounds in the right lower region. A Bartholin gland cyst was present, along with vaginitis due to the presence of Trichomonas.

Laboratory Findings.—The red blood cell count was 4,080,000, the hemoglobin content 11.6 Gm. and the white blood cell count 12,000, with 73 per cent polymorphonuclear cells and 4 per cent eosinophils. The sedimentation rate was 29 mm., and the nonprotein nitrogen, serum protein and albumin-globulin ratio were normal. Urinalysis revealed a trace of albumin, 10 to 20 white blood cells and 10 to 20 red blood cells per high power field. The sputum was negative for tubercle bacilli.

A roentgenogram of the chest revealed a dense shadow covering the entire lower portion of the right lung, with the outline of the diaphragm obscure (fig. 7 *A*).

Hospital Course.—A diagnosis of lung abscess was made, and during the first three days the temperature climbed to 103 F. in spite of the fact that penicillin was given intramuscularly and by inhalation. Bronchoscopy was performed on June 30, and large amounts of bloody sputum were aspirated. The temperature immediately returned to normal. This sputum did not contain acid-fast bacilli but showed alpha Streptococcus and Staphylococcus aureus on culture. The patient continued expectorating large amounts of dark brown, bloody pus, and on July 7 bronchoscopy was repeated and a large amount of the same type of sputum was aspirated and found to contain Endamoeba histolytica trophozoites. Consequently a diagnosis of amebic hepatic abscess with bronchohepatic fistula was made. A 10 day course of emetine and one course each of diodoquin® and chiniofon were given.

There was immediate response to emetine. The cough and expectoration subsided, and gradual clearing of the right lung took place (fig. 7 *B*). By July 30 the patient had gained 15 pounds (6.8 Kg.), and her temperature remained normal. The stools were negative for amebas, and at no time were we able to find amebas in the sputum. The complement fixation test for amebiasis gave negative results.

The Trichomonas vaginitis responded to treatment with lactic acid douches and floraquin® suppositories.

An otherwise uneventful convalescence was marred by the development of phlebothrombosis on August 29. On that date a bilateral femoral vein ligation was done, after which the convalescence was smooth.

The patient returned to this hospital on Dec. 9, 1948, complaining of cough and hemoptysis which had been present since September. In the interim she had been symptom free and had successfully undergone cesarean section in July 1948. Examination was essentially noncontributory. Roentgenograms of the chest revealed an increase in density in the right midlung field, which was thought to be due to fibrosis and was not active. Laboratory examinations, including

a complete blood count, urinalysis, determination of the nonprotein nitrogen, total protein and albumin-globulin ratio, serologic tests for syphilis and amebiasis, repeated examinations of the stool for parasites and smears and cultures of the sputum for acid-fast bacilli and amebas, all gave negative results or showed values which were within normal limits.

After the patient's admission she had a low grade fever and had a slight hemoptysis; bronchoscopy on December 15 revealed bloody secretion from the medial segment of the middle lobe of the right lung. She was treated conservatively with penicillin (intramuscularly and by inhalation), postural drainage, expectorants and bronchoscopy and under this regimen became asymptomatic. A bronchoscopic specimen on January 12 revealed Endamoeba gingivalis, but Endamoeba histolytica was never found again. A bronchogram revealed evidence of mild bronchiectasis, which was not considered to require surgical intervention. The patient was discharged on Feb. 21, 1949.

She was seen again in November 1949 and had been asymptomatic and gained weight. Examination at that time revealed nothing abnormal. In March 1950 she was working full time as a nurse and was entirely asymptomatic.

This case demonstrates the diagnostic difficulties involved in amebic abscess of the liver with pulmonary complications and the value of the awareness of the possibility of amebiasis in the diagnosis of pulmonary lesions of undetermined cause. It also shows the dramatic response of these lesions to administration of

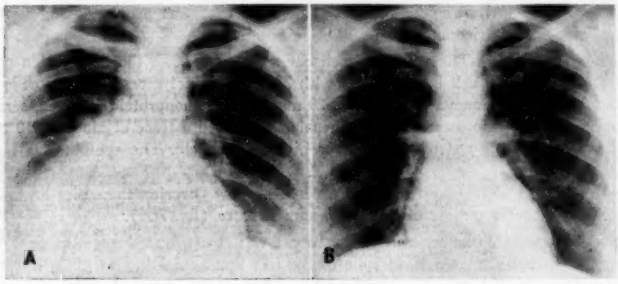

Fig. 7 (case 6).—*A*, amebic abscess of the liver with bronchohepatic fistula before treatment. Note elevation of the diaphragm and characteristic triangular shadow in lower right lung field. *B*, roentgenogram of the chest after conservative treatment with emetine and penicillin.

emetine hydrochloride. It is felt that the bronchiectasis manifested later was a residual effect of the disease.

COMMENT

Therapy for amebic abscess has finally undergone simplification. Before treatment is applied the diagnosis should either be established or be so likely that one could not reasonably question the institution of therapy. When hepatic amebic abscess is seriously suspected, penicillin in large dosages and emetine hydrochloride should be administered. Examination of the stools is important and must be done, but therapy must not be denied a patient because the stools are negative for pathogens.

In unproved cases the favorable response to emetine can be regarded as a factor of diagnostic significance. In many of our doubtful cases lowering of the temperature, slowing of pulse and betterment of the general condition occurred promptly although total control was not obtained. However, this favorable response is an extremely important observation in the matter of suggesting continued antiamebic therapy. We are of the opinion that there is often too much delay in therapy as the

result of procrastination about administering the drug emetine. We do not share the fear and alarm concerning its toxic properties found in medical and cardiological circles. One of us (R. F. B.) had seen hundreds of patients treated with emetine without a single deleterious effect, and no serious effects have been noted in the many obscure abdominal cases in which the drug has been used as a diagnostic aid. The great number of patients haphazardly given emetine during World War II and the absence of serious toxic effects suggest that the bad effects may be more academic than real. Sensible observation and respect for the toxicity of the drug are necessary. Unwarranted fear of its effect is seriously delaying the treatment of patients. It is contended also that if emetine and penicillin are administered in the early phase of amebic infections hepatic abscess will not be permitted to develop. A recent report by McVay and others[14] indicates that aureomycin, an antibiotic less toxic than emetine, may prove to be as efficient an amebacide as emetine. Improvement in intestinal amebiasis has been reported. However, one of our patients with hepatic abscess received a course of aureomycin, but ultimate control was not obtained until emetine was finally administered. It is hoped that a drug as simple as aureomycin will be forthcoming in the successful therapy of this disease. At the moment emetine is regarded as a specific; it is not as toxic as previously reported and should be administered promptly.

There appear to be four plans of therapy today. All include administration of emetine and penicillin plus eradication of the primary intestinal infection by the use of one of the iodine-containing amebacides.

Plan 1.—This is employed for hepatitis without abscess or in the stage of early suppuration. Penicillin and emetine (one or two courses) are given, followed by chiniofon or diodoquin.*

Plan 2.—The second plan is used for frank abscess with hepatomegaly. The therapy is administration of penicillin and emetine (one or two courses). If a mass is present, aspiration in the subcostal area with a long needle is recommended. Great care must be exercised to avoid injury to the gallbladder. One aspiration may suffice, but occasionally several are required.

Plan 3.—This is used for frank abscess without hepatomegaly. Penicillin and emetine (one or two courses) are given. If the response to drugs is not good after a reasonable period of trial or the clinical condition remains critical, laparotomy is advised. The abscess is located and drainage performed by (*a*) needle aspiration or (*b*) the use of a trocar and a closed drainage maneuver. If needle aspiration is the method of choice, careful location of abscess should be projected to the abdominal wall for future safe aspiration without further operation. Open drainage should never be employed.

Plan 4.—The fourth plan is employed for abscess with pleuropulmonary complications. The therapy consists of administration of penicillin and emetine (one or two courses) combined with postural and bronchoscopic drainage and repeated aspirations and is successful in the majority of cases of pleural amebiasis. As stated by Hughes and Westphal,[15] surgical procedures apart from aspiration are

14. McVay, L. V.; Laird, R. L., and Sprunt, D. H.: A Preliminary Report of the Successful Treatment of Amebiasis with Aureomycin, Science **109**:590-591, 1949.

15. Hughes, F. A., Jr., and Westphal, K. F.: Amebiasis with Pulmonary Involvement, Arch. Surg. **55**:304-315 (Sept.) 1947.

not indicated except for complications such as total empyema or bronchopleural fistula. In many cases closed drainage of empyema fluid will be successful, and in only a few will open drainage be necessitated.

Injections into the abscess cavity of antibiotics or emetine have not proved to be worth while enough to justify use.

SUMMARY

The therapy used in 16 cases of amebic abscess of the liver is briefly described. The present day therapy for this disease is successfully simplified. Awareness of the disease is an important factor in the diagnosis.

Therapy includes the utilization of emetine and penicillin; if administration of these drugs is instituted early in the course of the disease, control can often be secured without the aid of drainage. If the drugs fail to control the disease, simple needle aspiration or trocar closed aspiration is the method of choice. These are to be repeated as necessary. If the drugs fail and there is no hepatomegaly or other fluctuant mass, laparotomy is recommended to establish the location of the abscess in order that it may be drained by needle aspiration or trocar closed drainage method. Open drainage should not be employed.

CONGENITAL DILATATION OF THE COMMON BILE DUCT

Report of Two Cases in Children

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AND
C. E. MAGUIRE, M.D.
DETROIT

IN THE past 10 years at the Childrens Hospital of Michigan there have been two cases of choledochus cyst or congenital cystic dilatation of the common bile duct, in both of which treatment was successful. The increased number of case reports in the literature of this period indicates that this rare and interesting lesion is being recognized and treated more frequently and with better results.

Shallow, Eger and Wagner [1] in 1943 presented a comprehensive review of the literature in which a total of 175 authentic cases were reported. These authors [2] augmented that review in 1946 by the report of a case of their own and of six additional cases from the literature, bringing the total to 182 cases. A review of the more recent literature reveals case reports by Keeley, Kelsey, Davis, McLaughlin, Armanino, Irwin and Morison, Chesterman, Bleger and Boyer.[3] These with the two previously unreported cases presented here make a total of 192 authenticated cases.

The cases to be presented are those of a 5 year old Negro girl seen in the outpatient clinic in January 1938, on whom we have a 12 year follow-up, and a 1 year old white infant admitted in September 1948. The surgical management was different in each case, and three different procedures were utilized. The discussion to follow will attempt to evaluate the merit of the various surgical procedures in the light of immediate and subsequent sequelae.

From the Department of Surgery, Childrens Hospital of Michigan.

1. Shallow, T. A.; Eger, S. A., and Wagner, F. B., Jr.: Congenital Cystic Dilatation of the Common Bile Duct: Case Report and Review of Literature, Ann. Surg. **117**:355 (March) 1943.

2. Shallow, T. A.; Eger, S. A., and Wagner, F. B., Jr.: Congenital Cystic Dilatation of the Common Bile Duct: Follow-Up on Previously Reported Case and Report of Additional Case, Ann. Surg. **123**:119 (Jan.) 1946.

3. Keeley, J. L.: Congenital Cystic Dilatation of the Common Bile Duct, Arch. Surg. **56**: 508 (April) 1948. Kelsey, W. M.: Idiopathic Dilatation of the Common Bile Duct in Childhood, J. Pediat. **31**:211 (Aug.) 1947. Davis, C. E., Jr.: Choledochus Cyst: Case Report with Brief Comment, Ann. Surg. **128**:240 (Aug.) 1948. McLaughlin, E. F.: Choledochus Cyst, ibid. **123**:1047 (June) 1946. Armanino, L. P.: Idiopathic Dilatation of the Common Bile Duct with Coexistent Primary Hepatic Carcinoma: Report of a Case, Ann. Int. Med. **24**:714 (April) 1946. Irwin, S. T., and Morison, J. E.: Congenital Cyst of the Common Bile duct Containing Stones and Undergoing Cancerous Change, Brit. J. Surg. **32**:319 (Oct.) 1944. Chesterman, J. T.: Choledochus Cyst Complicating Pregnancy and the Puerperium, J. Obst. & Gynaec., Brit. Emp. **51**:512 (Dec.) 1944. Bleger, H. M., and Boyer, E. L.: Perforation of Choledochus Cyst with Biliary Peritonitis: Report of Case Submitted to 3-Stage Operation, Journal-Lancet **66**: 177 (June) 1946.

REPORT OF CASES

CASE 1.—M. J., a 5 year old Negro girl, was admitted to Childrens Hospital of Michigan on Jan. 12, 1938, with a history of pain in the right upper quadrant and vomiting. The patient had been well until one month prior to her admission, when she suddenly experienced severe right upper quadrant abdominal pain which lasted 10 to 15 minutes. During the ensuing few days she had two similar attacks which were associated with vomiting. The pain was intermittent in character, lasted a short period, was severest after meals and apparently did not radiate. On the day prior to the patient's admission to the hospital the pain became severer, remained constantly present and was only partially relieved when she lay on the right side with thighs flexed on the abdomen. Vomiting became more persistent, and for the 36 hours prior to admission no food had been retained. There had been some constipation since the onset of illness, but no abnormal stools were noted. The patient had been seen in medical clinic on two occasions with complaints referable to the present illness. Physical examination on both occasions had failed to disclose an abdominal mass or other contributory findings.

The physical examination revealed a well developed, acutely ill, dehydrated girl lying on the right side and holding her abdomen, with flexed thighs and complaining of abdominal pain. Her skin was warm and dry, and there was no cyanosis or icterus. The temperature was 99 F., the pulse rate 110 to 120 and the blood pressure 115/80. Abdominal examination revealed a visible and palpable mass in the right upper quadrant approximately the size of a large orange. This mass was firm, smooth, moved on respiration only and was tender. It filled the right upper quadrant from the anterior axillary line to the linea alba and extended from the costal margins to the umbilicus. The liver edge was palpable on respiration as separate from the tumor.

Laboratory studies revealed a hemoglobin content of 10 Gm., a red blood cell count of 6,000,000, a white blood cell count of 8,600, with 95 per cent polymorphonuclear cells and 5 per cent lymphocytes, and a negative reaction to the Kahn test. A roentgenogram of the abdomen revealed "a shadow of uniform density filling the right upper quadrant and displacing all bowel medially and inferiorly."

Laparotomy was performed on the night of admission by Dr. E. A. Osius. When the peritoneum was opened through an upper right rectus incision, the tumor was found to lie behind the second and third portions of the duodenum as well as the head of the pancreas. It was about the size of a large orange and was thought to be a pancreatic cyst. Aspiration of the cystic mass was performed and a clear bile-stained fluid obtained. The gallbladder was identified and found to be distended. The common duct could not be identified. The cyst was then opened near its superior border through the hepatocolic ligament and its contents evacuated. The cyst wall was smooth and glistening, and the examining finger could detect no communicating duct system. Because of the patient's poor condition it was thought best to marsupialize the cyst at this time. This procedure was rapidly carried out.

The patient's convalescence was essentially uneventful until the eleventh postoperative day, when a state of shock suddenly developed. This was successfully combated with intravenous administration of fluid and whole blood transfusion. The following day the presence of Koplik spots on the buccal mucosa and a typical generalized rash made possible a diagnosis of measles. Recovery from this intercurrent infection was uneventful.

There was a daily output of 500 to 1,000 cc. of bile through the fistula resulting from marsupialization of the cyst. This bile was collected by a gentle suction apparatus which made it possible to gavage the bile daily through a Levin tube and also prevented irritation of the abdominal wall by the drainage. This gavage was supplemented by oral administration of ox bile. Laboratory studies on the thirteenth postoperative day revealed the serum chloride content to be 586 mg. per 100 cc. and the total serum protein level 6.60 Gm. per 100 cc., with an albumin-globulin ratio of 2.7 to 1. On the twenty-sixth postoperative day the serum chloride level had dropped to 500 mg. Roentgen examination of the sinus tract at the site of marsupialization two months after operation revealed a cystic mass which would hold approximately 40 cc. of fluid. The sodium iodide filled several small ductlike structures which communicated with the main cyst near its superior aspect. None of the opaque material passed into the bowel at the time of injection; however, it was found to be present in the stools two days later. A Graham-Cole test revealed no concentration of dye in the cyst or the gallbladder.

The patient's condition gradually improved, so that by March 19, two months after the first operation, it was considered safe to perform the second stage procedure. This consisted of an excision of the sinus tract and an anastomosis of the cyst to the duodenum, the anastomosis being carried out between the origin of the sinus tract and the conveniently located proximal first portion of the duodenum. There were few adhesions present. The gallbladder was found to be collapsed and shrunken and the cyst approximately one half its previous size.

Subsequent to closure of the sinus and anastomosis of the cyst to the stomach, the improvement in the patient's condition was more rapid and convalescence uneventful. The color of the stools darkened, but there had been no acholic stools at any time. A Graham-Cole test was repeated three weeks after the second operation, and again there failed to be any concentration of dye in the biliary duct system. The patient was discharged in good condition on April 14, 1938, after 96 days of hospitalization.

Follow-Up Study.—The patient was seen regularly in the surgical outpatient department. She continued to have occasional episodes of mild pain in the right upper quadrant associated with vomiting and fever. The discomfort was colicky, cramping pain similar to that experienced at the onset of the present illness. Two of these episodes were severe enough to warrant readmission to the hospital (March 8 to March 22 and July 26 to Aug. 4, 1941). After each admission the patient was rechecked by means of roentgenograms of the upper gastrointestinal tract and the gallbladder. As on previous occasions, Graham-Cole tests revealed no concentration in the biliary tract and therefore were of no diagnostic value. However, the gastrointestinal roentgenograms revealed "a collection of barium and air in a large diverticulum off the proximal first portion of the duodenum." Retention of barium sulfate in the cyst was demonstrated roentgenologically 24 hours after its ingestion. There had been no appreciable change in the size of the cyst in the intervening two years. The episodes of pain and vomiting gradually subsided, and the patient was not seen in the clinic again, nor was it necessary to seek other medical attention for complaints referable to the choledochus cyst.

On Sept. 8, 1948, approximately 11 years after the onset of the symptoms of choledochus cyst, the patient was asked to return to the clinic. She was now 16 years of age, in the tenth grade in school, was 66 inches (167 cm.) in height and weighed 158 pounds (71.7 Kg.). She had been well and in good general health since the latter months of 1941, when she experienced the last episodes of pain in the right upper quadrant. Neither her diet nor activities had been restricted in any manner, and she apparently had no functional disturbances secondary to the presence of the remnant of the choledochus cyst. A Graham-Cole test was repeated at this time, and again no evidence of dye concentration could be demonstrated. There were, however, some linear gas shadows in the right upper quadrant which remained constant before and after a cleansing enema. These were believed to be in the biliary tract. On Oct. 7, 1948, a gastrointestinal series was carried out. The deformity of the proximal first portion of duodenum and the diverticulum in this region were again demonstrated. There was no change in size or shape of the diverticulum; barium sulfate and air were still present in the cyst at the time of a four hour examination.

Case 2.—R. M., a white male infant aged 1 year, was admitted to Children's Hospital on Sept. 10, 1948, with the chief complaints of irritability, anorexia, vomiting present for three days and an abdominal mass noted by the mother two days prior to admission.

The patient had been well until the onset of the present illness, which was initiated by anorexia, and an occasional small emesis following the ingestion of food. The vomiting was not projectile, and the material consisted of small portions of food in the undigested form and was frequently tinted a light green. The child became increasingly irritable and restless, crying and fussing except when held by the mother. Two days prior to admission the mother noticed that the right side of the abdomen seemed to be "swollen," and the child cried when moved or when pressure was applied in this area. The family physician confirmed the mother's impression that there was a mass in the right side of the abdomen and sent the child immediately to the hospital.

There was no history of previous illness or of similar episodes. The patient had a large normal-appearing bowel movement after a mild laxative the day prior to his admission. The family history revealed the child to be the youngest of four children, with two sisters 18 and 14

years of age and a brother 8 years old. There was no history of familial diseases, and although the parents and siblings were from Nashville, Tenn., the patient was born and had subsequently lived in Detroit.

Birth and development were essentially normal. The birth weight was 7 pounds, 8 ounces (3.2 Kg.). A normal spontaneous delivery with the mother under ether anesthesia had been carried out without preanesthetic medication. The infant gained on evaporated milk formula and was started on solid foods at 6 months. At the time of his admission he had 8 teeth and could stand alone and take several steps. There had been no immunizations and no communicable diseases.

Physical examination revealed the child to be a well developed and well nourished boy who appeared irritable, mildly dehydrated and in moderate discomfort. His skin was warm and dry and revealed several insect bites but no cyanosis or icterus. There was no unusual lymphadenopathy. The fontanelle was still slightly open, and on examination the eyes, ears, nose and throat appeared normal. The abdomen was slightly distended, and inspection revealed a "fulness" of the right upper quadrant. The entire abdomen was splinted by the child's crying, but the right upper quadant was noticeably more tender, and a firm, smooth mass approximately 4 inches (10 cm.) in diameter seemed to fill this entire region. The mass was movable on respiration and could be differentiated from the overhanging liver margin. Rectal examination revealed no masses, and the stool was normal in color and consistency.

Laboratory studies on admission revealed hemoglobin to be 10.8 Gm., the red blood cell count 3,980,000, the white blood cell count 8,900 and the differential count 60 neutrophils, 34 lymphocytes, 4 monocytes and 2 eosinophils. Urinalysis revealed a specific gravity of 1.020; the color was clear yellow and the p_H 5.0, and there was no albumin, sugar, cells or casts. A roentgenogram of the abdomen taken on admission revealed "a large soft tissue mass in the right upper region of the abdomen, presumably arising from the right kidney. No abnormal calcification is demonstrable, and the skeletal structures appear intact. There is no roentgen evidence of intestinal obstruction."

Hospital Course.—The day after admission there was no change in the patient's general condition despite parenteral administration of fluids. The temperature had remained normal, and further laboratory studies revealed the serum proteins to be 6.24 Gm. per 100 cc. and the albumin-globulin ratio 2.26 to 1. Intravenous pyelograms were done and again showed the appearance of a soft tissue mass in the right upper region of the abdomen displacing the gas-containing loops of bowel downward to the left. The dye appeared promptly in a normal concentration in both kidneys. The right kidney appeared rather large, but had a smooth sharp contour. The calices of the right kidney were poorly visualized. The appearance suggested either a diffuse infiltration of the right kidney or possibly pressure from an adjacent soft tissue mass. Roentgenograms of the skull were noncontributory.

On the second day of hospitalization the patient was taken to the operating room, open drop ether anesthesia was administered, venous section performed and whole blood transfusion started. The abdomen was opened through a right upper quadrant transrectus incision extending from the costal margins to a point midway between the umbilicus and the symphysis. When the peritoneum was opened a large mass was revealed in the right upper quadrant measuring approximately 4½ inches (11.4 cm.) in diameter. The tumor lay under the hepatic portion of the ascending and transverse colon and was entirely retroperitoneal. On the surface of the mass was a coiled duct 1 cm. in diameter which extended to a rudimentary gallbladder lying horizontally along the overhanging edge of the liver. The transverse and ascending colon were easily reflected medially off the mass. The cyst was readily separated from the retroperitoneal tissues laterally and inferiorly. It was then possible to palpate a normal kidney behind the cyst. The rudimentary cystic duct was clamped and cut and the dissection carried out on the superior and medial aspects of the cyst. Superiorly, another duct 1 cm. in diameter communicated with the cyst; this was demonstrated to be the common hepatic duct of approximately normal size and location. Inferiorly, the dissection was more difficult as the pancreas was firmly adherent to the mass. A small segment of patent common duct 1.5 cm. in length and 4 mm. in diameter was clamped, cut and ligated. No evidence of a communication with the pancreatic duct could be demonstrated, and therefore the stenotic stump was invaginated into the duodenal wall. The hepatic duct was then clamped and cut and the entire cyst removed with relative ease. The rudimentary gallbladder and cystic duct were also excised. The hepatic

duct was then freed and a section of size 8 French rubber catheter sutured into the hepatic duct with 000 plain surgical gut. An incision was made into the posterior-superior aspect of the duodenum at the junction of the first and second portions. The hepatic duct was inserted into the duodenum and fixed there by multiple interrupted 00000 silk sutures. There was no evidence of leak from the anastomosis and no unusual oozing, and the duodenum and colon resumed their normal positions. A Penrose drain was placed into Morison's pouch and the abdomen closed. Interrupted silk sutures were used for fascial closure. The patient received 150 cc. of whole blood during the operative procedure. His general condition had remained good throughout the two and one-half hour operation.

The postoperative course and the remaining period of hospitalization were uneventful. The patient's temperature returned to normal on the fourth postoperative day and remained normal thereafter. He was placed on clear fluids on the fourth postoperative day, and the Levin tube was clamped after oral administration of fluids. The Penrose drain was shortened and skin sutures removed on the seventh postoperative day. Blood and urinary amylase studies made postoperatively revealed no abnormalities which might indicate injury or obstruction of the pancreatic duct. On the eleventh postoperative day the drain was removed, and two days later the wound was dry and entirely healed. The patient was discharged on September 26, 14 days after operation.

Follow-Up Study.—The patient was seen at regular intervals in the surgical outpatient department and was free of any complaints. During the interview on the first visit, the mother stated that the patient had passed the piece of rubber catheter on September 30, 18 days after it was placed into the hepatic duct. He had not been limited in diet or activity and had been symptom free for the 12 months which had elapsed since resection of the choledochus cyst.

COMMENT

Incidence.—In 75 to 80 per cent of the reported cases congenital cyst of the common duct occurs in persons under 25 years of age. The majority of cases involve girls in the first and second decades of life, 60 per cent occurring in children under 10 years of age. The lesion is three times as common in girls as in boys. In older persons a careful review of the past history occasionally reveals previous episodes, with some symptoms characteristic of the lesion occurring long before its actual recognition and treatment. The cases presented here involved a 5 year old Negro girl and a white boy 1 year of age.

Etiology.—It is generally conceded that a congenital anomaly in the biliary tract is a necessary precursor to a choledochus cyst. There is still variance of opinions concerning the nature of the abnormality; however, the theory presented by Yotuyanagi [4] and subscribed to by Shallow, Eger, Wagner and others appears to be the most universally acceptable. Yotuyanagi based his explanation on embryologic principles and theorized an inequality in proliferation of the epithelial cells of the common duct, probably taking place at the stage of physiological epithelial occlusion. When canalization occurs later, a duct of unequal diameter results.

This theory is compatible with the occurrence of large cysts in young persons with a relatively short history of illness. In our second case a cyst approximately 10 cm. in diameter occurred in a child 1 year of age who had been ill only three days. The anomalous position of the gallbladder in this case further substantiates the hypothesis of formation of the cyst early in the embryologic development (fig. 1). Any of the mechanical theories presented would be acceptable only if symptoms

4. Yotuyanagi, S.: Contributions of the Aetiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile Duct with Report of 3 Cases: New Aetiological Theory Based on Supposed Unequal Epithelial Proliferation at Stage of Physiological Epithelial Occlusion of Primitive Choledochus, Gann **30**:601 (Oct.) 1936.

were apparent early, and with prompt exploration small cysts could be demonstrated. The valvelike formations demonstrated by Rostowzew and diagrammatically represented by Judd and Greene [5] are probably on the basis of torsion and angulation due to the weight and size of the preexisting cyst. It is when these mechanical factors eventually come into effect that symptoms of partial or complete intermittent obstruction become manifest. Heiliger, who observed a choledochus cyst in a stillborn fetus, concluded the primary anomaly to be a weakness in the wall of the common duct. Some tissue agenesis could be concomitant with an abnormal proliferative phase, resulting in a dilated as well as an atomic segment of common duct.

Symptoms and Diagnosis.—When the three cardinal symptoms of tumor (77 per cent), jaundice (70 per cent), and pain (59 per cent) are present, one is

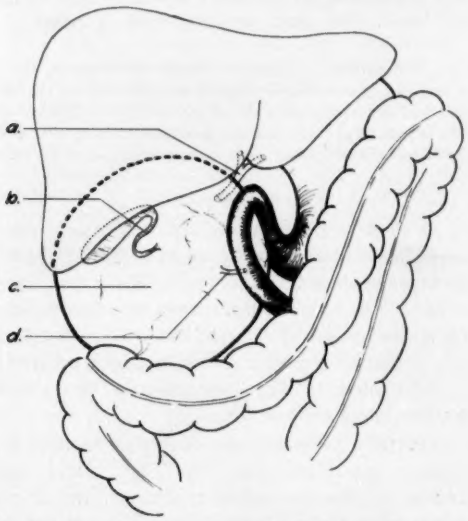

Fig. 1 (case 2).—The drawing shows diagrammatically the anatomic relationships between hepatic duct, cystic duct, choledochus cyst, undilated remnant of common duct and duodenum. The gallbladder is shown in its anomalous position along the overhanging edge of the liver. The letter *a* indicates the hepatic duct; *b*, cystic duct; *c*, choledochus cyst; *d*, common duct remnant.

prompted to consider biliary tract disease and, in the young person, to suspect biliary tract anomalies. The history frequently reveals previous episodes of transient jaundice along with other symptoms characteristic of mild obstruction or inflammatory seizures of the biliary duct system. In the absence of jaundice or of a history of jaundice, as in each of our cases, the diagnosis becomes more obscure.

Urograms frequently are of little assistance and occasionally may be misleading. Roentgenologic examination of the gastrointestinal tract reveals only a bowel-displacing mass in the right upper quadrant (fig. 2). Attempts at visualization of

5. Judd, E. S., and Greene, E. J.: Choledochus Cyst, Surg., Gynec. & Obst. **46**:317 (March) 1928.

the biliary tract by means of a Graham-Cole test are unsuccessful, for only rarely is there sufficient concentration of the dye to be apparent on the roentgenogram.

It therefore becomes necessary to consider choledochus cyst in the differential diagnosis of tumors in the right upper quadrant even though jaundice, the most significant of the triad, is not present.

Surgical Management.—The surgical management of choledochus cyst depends on the patient's ability to withstand a lengthy procedure. There are three fundamental methods of relieving the stasis, obstruction and infection when these are

Fig. 2 (case 2).—The roentgenogram shows the choledochus cyst as a bowel-displacing mass filling the entire right upper region of the abdomen.

present. The first and most expedient is marsupialization of the cyst wall. When the patient is acutely ill and the operation an emergency procedure, marsupialization may be indicated. Marsupialization, however, has been attended by generally poor results and should be looked on as only temporary. The maintenance of electrolyte balance and replacement therapy make a secondary procedure mandatory within a few weeks.

The second most expedient procedure, and the one utilized in the greatest number of cases, is anastomosis of the cyst wall to the duodenum or the upper portion of

the jejunum if it proves to be more accessible. Such a procedure was carried out as a second stage operation in our first case. This method of handling the cyst has met with uniformly good immediate results but is not entirely desirable because of the

Fig. 3 (case 1).—The roentgenogram on the left, taken several months postoperatively, shows the residual choledochus cyst filled with barium in a routine gastrointestinal series. The one on the right reveals barium and air in the cyst 24 hours after the barium meal.

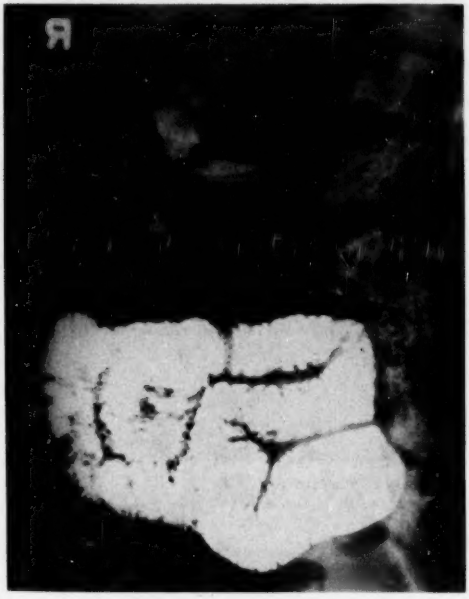

Fig. 4 (case 1).—Detail roentgenogram shows stasis in the residual choledochus cyst 12 years after anastomosis to the proximal first portion of the duodenum.

high incidence of sequelae secondary to stasis and subsequent ascending infection in the cyst and biliary tree.

The third and most desirable method is to excise the cyst and reestablish duct drainage directly into the duodenum or the upper portion of the jejunum. This

has been carried out by various means. Keeley performed a Rouz en Y anastomosis which proved satisfactory, but he recognized it as an undesirably formidable procedure. McLaughlin anastomosed the section of the dome of a choledochus cyst containing the cystic and hepatic duct to the duodenum, with satisfactory results. Davis found a well formed and apparently functioning gallbladder and carried out a cholecystoduodenostomy, with resultant recovery. Others have anastomosed the common hepatic duct or the right and left hepatic ducts to the duodenum, with gratifying results. It would seem that this method is the most desirable one to employ if at all possible. The cases reported in which the cyst was excised and a primary duct anastomosis carried out demonstrate a uniformly shorter period of morbidity and hospitalization and a relative absence of sequelae referable to the biliary tract.

The follow-up on those cases in which the choledochus cyst was anastomosed to the upper part of the small bowel reveal a high incidence of recurrent seizures characteristic of stasis, infections, lithiasis and obstruction. The patient in our first case had recurrent episodes of pain in the right upper quadrant, nausea, vomiting and fever over a period of three and one-half years after her discharge from the hospital, and now, 12 years later, there is still roentgenologic evidence of a pouch off the proximal duodenum which contains air and barium sulfate 24 hours after a series of gastrointestinal roentgenograms (figs. 3 and 4). Our second case represents one in which excision of the cyst and anastomosis of the hepatic duct to the duodenum resulted in an absence of sequelae and permitted a normal rate of growth and development.

SUMMARY

Two previously unreported cases of choledochus cyst occurring in young children are presented. The importance of considering choledochus cyst in the differential diagnosis of pain or tumor in the right upper quadrant in the absence of jaundice is emphasized. The necessity of removing the cyst and establishing a stasis-free direct anastomosis between the hepatic ducts and the duodenum is pointed out as the method of choice because of the low incidence of sequelae.

NOTE.—Since the preparation of this report one other case of choledochus cyst has been observed by one of us (C. E. M.). The patient was a 7 year old Negro girl who was operated on on May 20, 1950. This child had a large choledochus cyst measuring 4 inches (10 cm.) in diameter. It was of such a size that its removal was not feasible. An anastomosis of the cyst to the second portion of the duodenum was performed, and the child made an uneventful recovery. Sufficient time for evaluation of the final result has not elapsed, but to date the patient has been symptom free.

Case Reports

BONE BRIDGING WITH OPPOSING MASSIVE HEMICYLINDRICAL GRAFTS

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There have been numerous methods used in bridging large bone defects. A review of the literature shows as many different technics as authors writing articles.[1] Oscar L. Miller states: "All types, kinds, and sizes of grafts have had their supporters. Operations have succeeded and failed for each other."[2]

It is well known that the success of a bone graft depends on many factors; some are known and some remain a veritable mystery. Success may occur when the odds are prohibitive and failure ensue in cases appearing to be ideal for grafting. There are, however, three basic procedures used in bridging bone defects: (1) whole fibular transplants,[1j] (2) dual onlay tibial grafts[1j] and (3) the most recent technic developed by Flanagan and Burem, opposing massive hemicylindrical grafts taken from the affected bone, used especially in reconstructing defects of the tibia and the femur.[3] This procedure is based on principles as outlined by Hey Groves and by Gill.

The whole fibular graft usually provides an ideal way of bridging defects, especially in the radius, ulna and humerus. It is used also in the lower part of the leg; however, in adults it has been found unsatisfactory since the fibula does not usually hypertrophy sufficiently to withstand the stress and strain of weight bearing. The tubular construction of the fibula provides a graft which

1. (*a*) Compere, E. L.: Massive Bone Graft in the Treatment of Ununited Fractures, Repair of Defects in Long Bones and Fusion of Spine, S. Clin. North America **13**:1261-1273, (Oct.) 1933. (*b*) Carpenter, G. K.; Rosenfield, R. T., and Mech, K. F.: Restoration of Bone Strength with Reinforcement Bone Grafts, J. Bone & Joint Surg. **28**:692-697 (Oct.) 1946. (*c*) Farrow, R. C.: Summary of Results of Bone Grafting for War Injuries, J. Bone & Joint Surg. **30-A**:31-39 (Jan.) 1948. (*d*) Gibson, A., and Loadman, B.: Bridging of Bone Defects, J. Bone & Joint Surg. **30-A**:381-396 (April) 1948. (*e*) King, B. B.: Experiences with Bone Grafting Procedures for the Treatment of Battle Casualties and War Injuries, Am. J. Surg. **24**:129-135 (Aug.) 1947. (*f*) Miller, R. C., and Phalen, G. S.: Repair of Defects of the Radius with Fibular Bone Grafts, J. Bone & Joint Surg. **29**:629-636 (July) 1947. (*g*) Moore, J. R.: Massive Bone Defects in Compound Wounds, J. Internat. Coll. Surgeons **10**:274-286 (May-June) 1947. (*h*) Murphy, F. G.: Intramedullary Onlay Grafts for Defects Resulting from Shattering Fractures, J. Bone & Joint Surg. **29**:1068-1074 (Oct.) 1947. (*i*) Parnall, E.: Gap Bone Grafts, Rocky Mountain M. J. **44**:711-713 (Sept.) 1947. (*j*) Moore, J. R.: Transplantation of Fibula to Replace Defect of Tibia, J. Bone & Joint Surg. **26**:455, 1944.

2. Miller, O. L.: Massive Bone Grafts: Report of Cases, South. M. J. **25**: 211-218 (March) 1932.

3. Flanagan, J. J., and Burem, H. S.: Reconstruction of Defects of Tibia and Femur with Apposing Massive Grafts from the Affected Bone, J. Bone & Joint Surg. **29**:587-597 (July) 1947.

is stronger than tibial grafts and also provides a more normal form to replace defects, thus facilitating closure of the wound since it does not increase the cubic content of the extremity.

Dual onlay grafts have some advantages over fibular grafts in that it is possible to avoid the hourglass constriction which commonly occurs with other technics. This procedure also maintains the diameter of the grafted bone. Dual onlay grafts can also be used in both the upper and lower extremities. They do, however, increase the cubic content of the extremity and may result in necessitating wound closure under considerable tension. It has been found that the partial absorption of one graft in cases of dual onlay does not necessarily mean failure, since the second graft may take and permit union.

Hemicylindrical opposing massive grafts are based on principles outlined by Hey Groves and by Gill. The present technic developed by Flanagan and Burem may well be the answer to the treatment of large defects in the lower extremities. This procedure, however, is not without its disadvantages. Flanagan and Burem, who developed this technic, have presented an interesting series of cases showing what can be done by a well planned and skilfully carried out procedure in bridging large bone defects. There should be no doubt that they have made a contribution in the progress of bone surgery. Certainly their results prove the soundness of their principles. By opposing hemicylindrical grafts taken from the affected bone, they have been able to reconstruct the tubular architecture of the bone at the site of the defect, thereby maintaining the continuity of the medullary canal and also preserving tubular strength. Their results are a testimony to the fact that the two opposing half cylinder grafts become firmly fixed to each other and to the host bone. Three distinct operative procedures have been developed for the tibia and femur according to the level of the defect as reported by Flanagan and Burem.[3]

As Brown has shown, the success of any reconstruction procedure is in direct ratio to the physical condition of the patient and the adequacy of skin coverage through which operation is to be done.[4] All the usual preliminary considerations prior to bone grafting such as elimination of infection, repair of skin defects, excision of scars and replacement with appropriate skin and physical reconditioning should, of course, be observed if success is to be attained.[4] It should also be emphasized that bone surgery should not be attempted for a period of three months after replacement of skin grafts with full-thickness skin grafts by means of either pedicle, tube or local skin flaps. Horwitz advises waiting six to eight months in view of Farrow's analyses of incidents of infection in his series of bone graft operations.[5] The technic of Flanagan and Burem, as has been described, is applicable to cases in which less radical procedures have been tried without success or which do not lend themselves to ordinary methods because of the length of the defect. A report is presented here illustrating the use of this technic in a case in which the use of a fibular graft was previously attempted.

REPORT OF A CASE

L. G. T., a 30 year old white man, suffered a severely comminuted, compound fracture of the middle third of his left leg on Jan. 1, 1942, when, while pushing a car to get it started, he was struck by an oncoming car which crushed his leg between the bumpers. He was treated elsewhere by skeletal traction through

4. Brown, J. B.: Surface Repair of Compound Injuries, J. Bone & Joint Surg. **26**:448-454 (July) 1944.

5. Horwitz, T.: The Behavior of Bone Grafts, Surg., Gynec. & Obst. **89**: 310-316 (Sept.) 1949. Farrow.[1c]

the os calcis. A severe infection of the wound at the fracture site ensued, and, as the patient stated, "gas gangrene set in." Amputation was advised, but since the patient was an Atlas pupil, had a good muscular physique and was proud of his build, he firmly refused this treatment in spite of the threat to his life.

Longitudinal incisions for drainage were made through the entire length of his leg, extending to above the knee. The leg drained profusely, and the patient rapidly lost weight. On April 11, 1942, the drainage had subsided and a long leg plaster cast was applied elsewhere. He underwent repeated changes of the cast, at which times protruding sequestrums were removed. Finally, on Aug. 27, 1943,

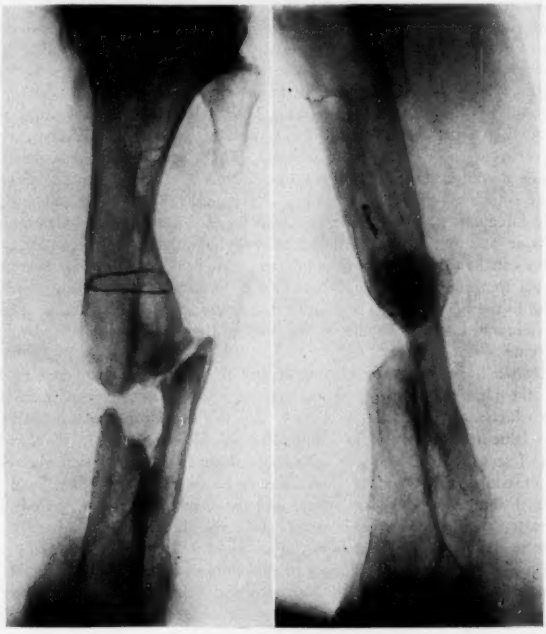

Fig. 1.—Preoperative bone defect showing pseudoarthrosis of fractured fibular graft and tibial defect.

the wound appeared to be healed. He was fitted with a leather and steel form-fitting brace and instructed to start weight bearing.

The patient stated that without the brace the leg was flail. He got along with the brace with considerable difficulty. On Dec. 29, 1945, he was hospitalized and a modified Huntington procedure was done. He wore a plaster cast for twelve weeks, and then a walking cast was applied on March 15, 1946, and he was advised to start weight bearing gradually. On July 22, 1946, the cast was removed and he evidently was instructed to continue weight bearing. Four days later, while walking, the graft fractured with a sudden loud crack, "like that of a rifle shot." He returned to the hospital, where roentgenograms revealed a

fracture of the transplanted fibula at the site where a transfixing screw had been placed to hold the fibula to the tibia. This screw was removed, and a long leg cast was applied. In spite of prolonged immobilization, a pseudoarthrosis developed at the fracture site.

The patient was first seen in this office in September 1948. The leg was flail in its middle third, and there was dense scarring of the skin over the anteromedial aspect. The ankle joint was fused in about 10 degrees equinus, and there

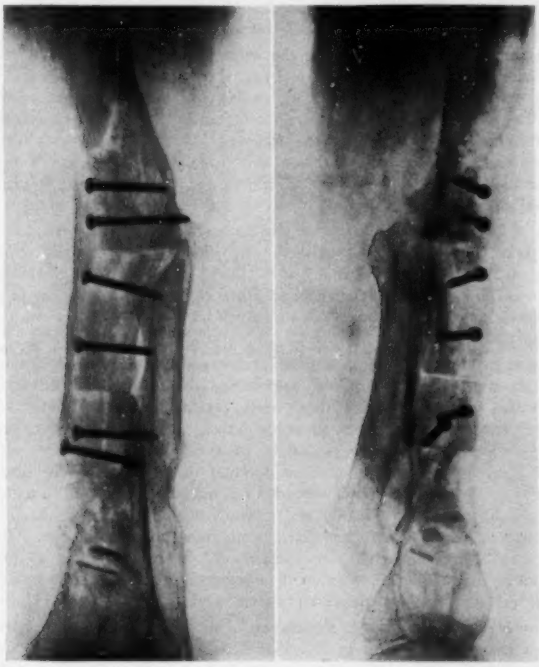

Fig. 2.—Roentgenograms taken immediately after operation showing squaring of bone ends, rebedding of grafts across defect and filling of lower residual donor defect with iliac chips and upper donor defect with iliac segment graft.

was good motion and stability of the knee joint. Roentgenograms revealed a defect of the middle third of the tibia, with the bone ends tapering and sclerosed.

The fibula had been swung over by surgical means to the proximal tibial fragment in an effort to bridge the tibial defect. The fibula had fractured, however, and there was now a pseudoarthrosis. The fibula had hypertrophied considerably. There was notable decalcification and atrophy of all the bones of the foot, ankle and leg.

The risks of the Flanagan-Burem operation were discussed with the patient, and he agreed to whatever the consequences might be. On Nov. 16, 1948, the

dense scar tissue over the anteromedial aspect of the leg was excised, long incisions paralleling the wound from which the scar had been excised were made and the intervening skin was undermined and slid together so that the wound was now covered with healthy skin and closed without undue tension. The gaping supplementary incisions were closed with thick split-thickness grafts taken from the abdomen by means of the Padgett dermatome. The skin grafts and the wound healed per primam.

Three months later the patient was readmitted to the hospital and opposing hemicylindrical massive bone graft reconstruction, as described by Flanagan and Burem, was done. A modified type 3 method was used.

The surgical approach was over the anteromedial aspect of the tibia through the incisional scar from which the dense scar tissue had been excised. The incision extended the entire length of the leg from the knee joint to the ankle joint. The periosteum was incised and reflected only from the side from which the hemicylindrical graft was to be removed. The shaft of the affected bone was thus exposed, working both above and below toward the site of the defect. All scar tissue presenting itself was removed, and the intervening tissue between the tibial defect and the pseudoarthrosis of the fibula was also excised.

The tibial bone ends were freed and squared off with a hand saw back to normal bone, and all poorly nourished bone was thereby removed. With fixed traction on the extremity by means of a Hawley table, the defect was measured (2½ inches [6.35 cm.]) and the required grafts determined. Grafts were removed subperiosteally, care being taken not to disturb the periosteum over the remaining sound portions of the shaft.

Longitudinal cuts of the superficial cortex were made with the motor saw. Cross cuts were made by drilling holes along the desired line of cut through both cortices and then joining these holes carefully with the motor saw. As cautioned, care is taken to complete the cross cut before the deep cortex is cut longitudinally, since there is danger of splitting the shaft through to the adjacent joint or of breaking it at the level of the cross cut. The deep cortex was cut by drilling multiple holes along the desired plane of cut and then connecting these holes by means of a mallet and a thin osteotome. The grafts were then rebedded as indicated (fig. 2) and fixed firmly with vitallium screws. The distal defect created at the donor site was filled in with iliac bone blocks and chips and the proximal defect filled in with an iliac segment graft about 4 inches (10 cm.) in length taken from the patient's right iliac crest.

Figure 3 reveals the greater stimulation of osteogenesis caused by bone blocks and chips than by a segment graft. Iliac bone blocks and bone chips were also placed around the site of the pseudoarthrosis between the fibula and the tibia. Figure 3 also shows the stimulation of healing at this site. The periosteum was closed over where it had been reflected and the wound closed in the usual manner. A plaster hip spica was then applied. Penicillin and streptomycin were both given for a period of one week postoperatively.

The patient had an uneventful course. Two weeks postoperatively a window was cut from the cast and the skin sutures removed. The wound had healed per primam. Thirteen weeks later the hip spica was removed, and roentgenograms revealed the grafts to be holding their position well, with osteogenesis and union progressing satisfactorily (fig. 3). A long leg plaster cast with walking iron was applied, and the patient was instructed to start weight bearing gradually with the aid of crutches. Repeated roentgenograms were taken during the ensuing several days and weeks to check on the stability of the grafts. The patient (and

Fig. 3.—Anteroposterior and lateral views three months after operation showing osteogenesis stimulated by iliac bone chips at lower donor defect and site of pseudoarthrosis of fibula. Note greater stimulation of osteogenesis by bone chips over iliac segment graft in upper donor defect.

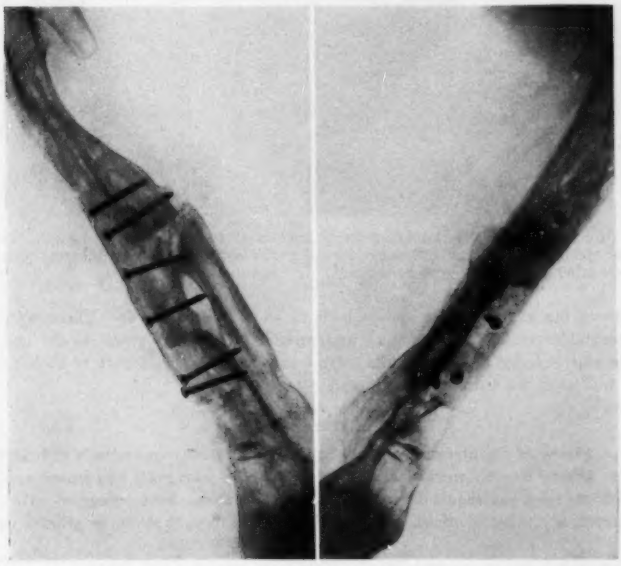

Fig. 4.—Anteroposterior and lateral views seven months after operation.

perhaps the surgeon) was fearful that the grafts might collapse. They maintained their position, however, without the least evidence of stress or strain.

On July 29 the cast was removed, and a long leg brace was fitted. Roentgenograms revealed osteogenesis and union still progressing.

This was the first time in over seven years that the patient had worn a shoe on his left foot. He walked with crutches for several weeks and then started using a cane. Previous to surgical intervention there had been severe thickening and induration of the entire leg. With continued use of the extremity, the thickening and induration gradually disappeared. The skin became soft and pliable and regained its normal color and texture. At this time the patient is walking

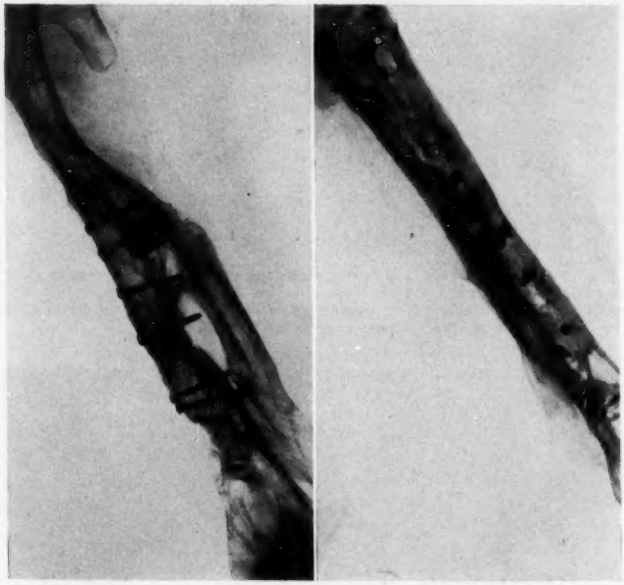

Fig. 5.—Anteroposterior and lateral views taken one year after operation. Note that the opposing massive hemicylindrical grafts are becoming an integral part of each other and of the host bone itself.

without the aid of a cane and is back to work as a plasterer. There was no measurable residual shortening of the extremity. Roentgenograms at the end of one year revealed that the grafts were becoming an integral part of each other as well as of the host bone itself.

SUMMARY

A review of the literature reveals that there are numerous methods of bridging bone defects. Reports would indicate that any type of bone graft may be successful; however, surgeons should keep in mind that operations have succeeded in some instances and failed in others. Considerable detailed thought should be given to each

individual case in order to work out the indications for the use of a particular procedure, keeping in mind the respective merits of various procedures as applied to the case involved. The state of healing processes and influencing factors should be given proper consideration; the intactness of periosteum, necessity of interfering with intermediary callus and sclerosing bone ends, need of internal fixation, use of inlay, onlay, single or dual grafts and of cortical or cancellous bone graft and the presence of infection, scar tissue and unhealthy skin each should be carefully considered if healing is to be given the optimum chance to occur.[6] Adequate and proper support of the grafted extremity and the use of braces during early weight bearing should be maintained for a sufficient length of time to stimulate the development and strength of osteogenesis. (Personal communication with Dr. Flanagan.) A successful case of bone bridging in the tibia with opposing massive hemicylindrical grafts is presented.

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6. Abbott, L. C.; Schottstaedt, E. R.; Saunders, J. B. De C M., and Bost, F. C.: The Evaluation of Cortical and Cancellous Bone as Grafting Material: Clinical and Experimental Study, J. Bone & Joint Surg. **29**:381-414 (April) 1947. Albee, F. H.: The Autogenous Bone Graft in the Treatment of Nonunion of Fractures, Internat. J. Med. & Surg. **45**:209-216 (May) 1932. Abbott, L. C.: The Use of Iliac Bone in the Treatment of Ununited Fractures, in Lectures on Reconstruction Surgery of the Extremity, American Academy of Orthopaedic Surgeons, Ann Arbor, Mich., Edwards Brothers, Inc., 1944, pp. 13-22. Bishop, W. A., Jr.; Stauffer, R. C., and Swenson, A. L.: Bone Grafts: End-Result Study of Healing Time, J. Bone & Joint Surg. **29**:961-970 (Oct.) 1947.

TORSION OF AN ECTOPIC OVARIAN CYST COMPLICATING EARLY PREGNANCY

Discussion of Unusual Anatomy and Etiology

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AND
JEROME G. DAVIS, M.D.
BROOKLYN

Congenital abnormalities of the female genital tract are relatively common. Torsion of an ovarian cyst complicating pregnancy is frequently encountered. However, a twisted undescended ovarian cyst whose stalk passes through an open intersigmoid fossa has not been previously reported, as far as we could discover.

A review of the literature revealed many cases of ectopia of the ovary, but almost invariably the ectopic ovaries were situated in the inguinal region. Packard and Rector [1] in 1948 collected more than 300 cases of inguinal ectopia of the ovary. Occasionally [2] an ovarian cyst is found in an inguinal hernial sac. Van Meurs [3] reported strangulation of an ovary and a fallopian tube in an obturator hernia. Although many anatomic variations were noted, there was no reference to an ovary herniating through the intersigmoid fossa.

REPORT OF CASE

Mrs. E. S., a white woman 22 years old, a nullipara, was examined on Oct. 7, 1948, with a history of having had her last menstrual period on Aug. 22, 1948. Her menstrual history was 12 years, 25 day interval, 4 day duration, with no irregularities. Her past history was noncontributory. The general physical condition and laboratory findings were normal. A pelvic examination revealed the cervix to the left with the uterus slightly enlarged and softened. There was a cystic mass in the left adnexal region about 5 cm. in diameter, movable and nontender.

The impression at this time was that we were dealing with an early intrauterine gestation complicated by a left ovarian cyst. Because of the small size of the cyst, it was felt that observation rather than surgical intervention was indicated. The patient was reexamined on Nov. 11, 1948, at which time a mass was noted suprapubically and toward the left. This was irregularly higher toward the left than medially. There were no complaints.

On November 25 we were called to the patient's home when she experienced the sudden onset of sharp, lancinating pain in the lower abdominal area, chiefly in the left lower quadrant, associated with nausea and repeated violent vomiting and chills. The temperature was 99 F., the pulse rate 100 and the blood pressure 110/70. The patient appeared acutely ill and in severe pain. A change was noted on abdominal examination. There was a rather tense, globular, cystic mass about 15 cm. in diameter, situated in the left hypochondriac region at the site usually occupied by an enlarged spleen. The previous irregularity in the lower abdominal area had disappeared; the fundus extended about 5 cm. above the symphysis. There were moderate tenderness, muscle spasm and rebound tenderness across the lower part of the abdomen, more marked in the left lower quadrant. Pelvic examination revealed an increase in the size of the uterus consistent with gestation of about 12 weeks. The cervix was softened and tender on motion; the left ovarian cyst previously noted was not palpable in the adnexal position. A diagnosis of twisted ovarian cyst complicating early pregnancy was made, and immediate operation was performed.

From the Prospect Heights Hospital.

1. Packard, F. B., and Rector, E. M.: Inguinal Ectopia of Ovary, Northwest Med. **47**:354-355 (May) 1948.

2. Fusaro, W. J.: Ovarian Cyst in Content of Inguinal Hernial Sac, New York State J. Med. **46**:1024-1025 (May 1) 1946.

3. Van Meurs, D. P.: Strangulation of Ovary and Fallopian Tube in an Obturated Hernia, Brit. J. Surg. **32**:539-540 (April) 1945.

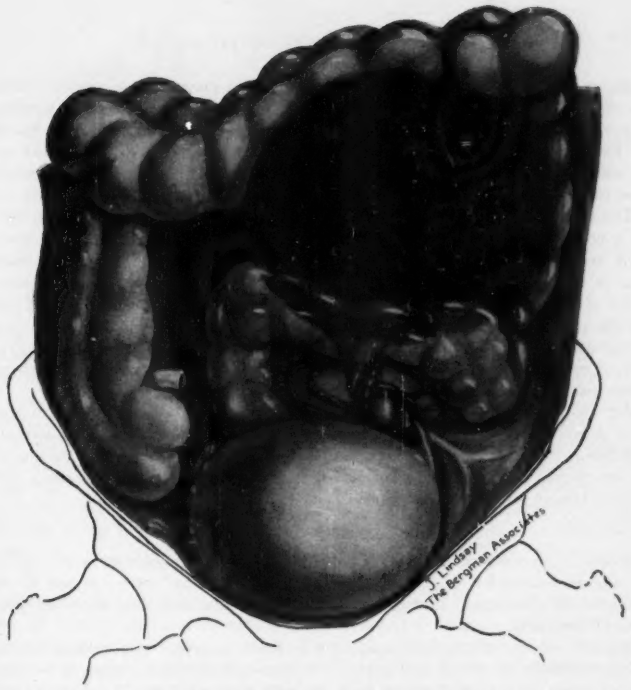

Fig. 1.—The twisted pedicle is seen passing through the intersigmoid fossa, converting it into a canal. The ovarian cyst occupies the left upper quadrant of the abdomen.

Fig. 2 (Treves).—The sigmoid is elevated to show the mesosigmoid and the location of the intersigmoid fossa.

The uterus was found to be enlarged in keeping with a pregnancy of about 12 weeks, with a normal right tube and ovary. There was a twisted left ovarian cyst (one and a half turns of the pedicle), with hemorrhage into the cyst, located in the left upper quadrant of the abdomen (fig. 1). The cyst measured about 17 by 15 cm. There was an opening of the sigmoid mesentery (fig. 2), which was oval and measured 3 by 2 cm. Through this opening passed the stalk of the ovary consisting of utero-ovarian infundibulopelvic ligaments, the fallopian tube and associated vessels. The stalk was clamped on either side of the sigmoid opening and divided, and the ovarian cyst and a portion of the tube were removed. The proximal stump was ligatured with double sutures. A continuous atraumatic suture was used for the congenital mesenteric hiatus. The postoperative course was normal, the wound healing by primary intention. The patient was allowed out of bed on the second postoperative day. Fifty milligrams of progesterone was given intramuscularly daily for eight days, followed by 50 mg. orally for a month.

The pathologist reported a cystic mass 17 cm. in its greatest diameter, to which was attached a segment of tube 4 cm. in length. The cyst was multilocular and contained mucinous substance. The pathological diagnosis was pseudomucinous cystadenoma of the ovary.

On May 20, 1949, after a normal labor of nine hours, an 8 pound 2 ounce (3.6 Kg.) male infant was delivered by low forceps, aided by episiotomy with the patient under nitrous oxide–ether anesthesia. The postpartum course was uneventful. On June 28, 1949, a check-up revealed that the patient had had a normal menstrual period. The wound was well healed, and pelvic examination revealed no adnexal masses.

COMMENT

The finding of an abnormally located, twisted ovarian cyst in a pregnant woman raised questions of possible reasons for the unusual location in the abdominal cavity. It was believed that a herniation of the ovary could have occurred, but it was more likely that there had been failure of descent of the ovary.

The presence of an intersigmoid fossa was in itself a rarity. An opening has not been described in textbooks nor in the literature. The opening found here was of such a size that a normal adult ovary could have passed through, but with great difficulty. If the ovary were cystic and slightly enlarged, this would have been impossible. We assume, therefore, that this was in truth a case of failure of descent of the ovary. It occurred on the left side, where there may be a natural barrier to the descent of the ovary, that is the mesocolon.[4]

The ovarian cyst was discovered six weeks after the last menstrual period and was probably of long duration. During pregnancy, with enlargement and ascent of the uterus, there was traction on the infundibulopelvic ligament with its contained blood vessels. Ovarian circulation was disturbed and cyst formation accelerated. Torsion may have finally occurred when the pelvic region of the colon was moved by a rush of its contents and the rectus muscles contracted in a well timed sequence.

SUMMARY

A case of torsion of a congenitally ectopic cystic ovary complicating early pregnancy is presented. It has been concluded that this was a true congenital lesion, discovered because of the physiological changes occurring in pregnancy which gave rise to torsion and hemorrhage. Explanation is thus offered for a striking situation, the origin of which was by no means clear.

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4. Treves, F.: Surgical Applied Anatomy, revised by L. Rogers, ed. 11, Philadelphia, Lea & Febiger, 1948, p. 349. Hamilton, W. J.; Boyd, J. D., and Mossman, H. W.: Human Embryology (Prenatal Development of Form and Function), Baltimore, Williams & Wilkins Company, 1945, pp. 202 and 219. Arey, L. B.: Developmental Anatomy: A Textbook and Laboratory Manual of Embryology, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 219 and 247.

HEPAR LOBATUM WITH PORTAL HYPERTENSION SUCCESSFULLY TREATED BY PORTACAVAL ANASTOMOSIS

JOHN H. LAZZARI, M.D.
AND
FRANK J. RACK, M.D.
CLEVELAND

Interest in portal cirrhosis has been greatly stimulated by the recent advances in the nutritional aspects of the problem [1] and by the reports of Whipple,[2] Blakemore [3] and Blalock [4] establishing the feasibility of a direct attack on the abnormal pressure relationships between the portal and caval systems of veins in this condition.

Most cases of intrahepatic portal obstruction and portal hypertension represent instances of Laennec's cirrhosis. However, other conditions occasionally produce portal hypertension, and these include so-called postnecrotic cirrhosis,[1] cirrhosis secondary to the taking of drugs [5] and syphilitic cirrhosis. The utilization of a portacaval anastomosis for portal hypertension resulting from this last condition, hepar lobatum, has not been previously reported. For this reason we present a case of hepar lobatum recently treated at this hospital by means of a portacaval anastomosis.

REPORT OF CASE

M. P., a 54 year old white woman, was transferred to Cleveland City Hospital on Nov. 10, 1949, because of recurrent massive hemorrhage from esophageal varices. The patient had been well until one year before her admission, when she noted gradual swelling of the abdomen and a steady increase in weight. During the eight months previous to her last hospitalization she had had three episodes of massive hemorrhage in the upper gastrointestinal tract, each time requiring hospitalization and multiple transfusions. In March of 1949, during the first hospitalization, liver function tests were found to elicit normal reactions but there was definite roentgenologic evidence of esophageal varices. The patient was known to have a positive Wassermann reaction, but there was no history of alcoholism or of any vitamin deficiencies.

Examination of the patient on her admission to this hospital revealed her to be in no acute or chronic distress. The abdomen was distended with fluid and bulging in the flanks. The red blood cell count was 2,500,000, with 10 Gm. of hemoglobin per 100 cc., and the white blood cell count was 5,100, with 59 per cent polymorphonuclear cells, 7 per cent stab forms, 16 per cent lymphocytes, 7 per cent monocytes, 10 per cent basophils and 1 per cent eosinophils. The platelets were normal. The total protein value was 6.1 Gm., with an albumin-globulin ratio of 1.91. The prothrombin time was 23 seconds (normal, 17 to 19 seconds), and sulfobromophthalein retention was 24 per cent after one hour (normal, 5 per cent). Thymol turbidity was

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From the Department of Surgery of Cleveland City Hospital and the School of Medicine, Western Reserve University.

1. Patek, A. J., Jr.; Post, J.; Ratinoff, O. D.; Mankin, H., and Hillman, R. W.: Dietary Treatment of Cirrhosis of the Liver: Results in 124 Patients Observed During 10 Year Period, J. A. M. A. **138**:543 (Oct. 23) 1948.

2. Whipple, A. O.: The Problem of Portal Hypertension in Relation to the Hepato-Splenopathies, Ann. Surg. **122**:449, 1945.

3. Blakemore, A. H.: Indications for Portacaval Anastomosis: Analysis of Cases, Surg., Gynec. & Obst. **84**:645, 1947.

4. Blalock, A.: The Use of Shunt or By-Pass Operations in the Treatment of Certain Circulatory Disorders Including Portal Hypertension and Pulmonary Stenosis, Ann. Surg. **125**:129, 1947.

5. Osler, W.: Principles and Practice of Medicine, edited by H. A. Christian, ed. 15, New York, D. Appleton-Century Company, Inc., 1944, pp. 411 and 757.

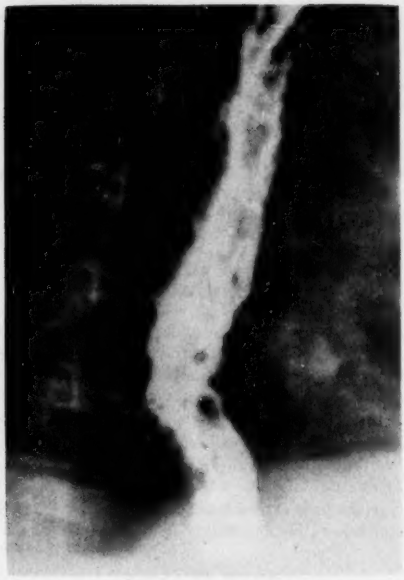

Fig. 1.—Preoperative roentgenogram presenting evidence of esophageal varices.

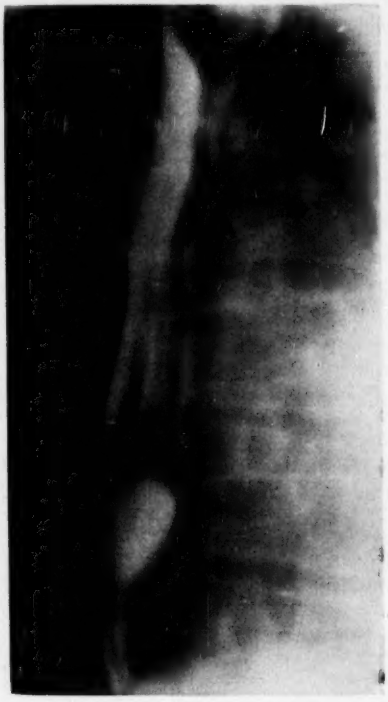

Fig. 2.—Roentgenogram made eight months after operation presenting little evidence of varices previously demonstrated.

3.5 units (normal, 3 to 5 units), and there was 63 per cent hippuric acid excretion (normal, 75 per cent). The values for cephalin flocculation were 0 and 1 plus (24 and 48 hours) on one occasion and 3 plus and 3 plus on another occasion. The Kline diagnostic and exclusion tests of the blood gave a 4 plus reaction, but the Wassermann test of the blood and the Kline test of the spinal fluid elicited negative reactions. There was roentgenologic evidence of esophageal varices (fig. 1).

On the eighth hospital day paracentesis yielded 3,000 cc. of clear fluid, and examination immediately afterward revealed a questionably palpable spleen and liver. On the nineteenth day operation was performed.

Operative Note.—With the patient under gas-oxygen-ether anesthesia and an intratracheal tube in place, a combined thoracoabdominal incision was made on the right opening the peritoneal and right pleural cavities. The diaphragm was divided and the liver displaced into the chest.

Fig. 3.—Sections of a liver biopsy specimen revealing necrosis, fibrosis and plasma cell and lymphocytic infiltration consistent with the diagnosis of hepar lobatum.

The gallbladder was found to be full of small stones and was removed in routine fashion. The liver was found to be enlarged with large nodules measuring 10 to 15 cm. over its surface. Between nodules there was contraction of scar tissue, giving the liver the appearance of a hepar lobatum. The portal vein and the vena cava were dissected free and the many collateral vessels encountered during this dissection ligated and divided. A shunt was created between the portal vein and the vena cava, the Smith Freeman clamp[6] being employed to hold the vessels. The anastomosis was made with 00000 arterial silk, a single continuous over-and-over suture being utilized. An opening between the two vessels measuring about 13 mm. was

6. Freeman, S.: Studies on Eck Fistulas in Dogs: A Simple Technique for Preparation of a Portacaval Anastomosis with the Aid of a Clamp, Surg., Gynec. & Obst. **87**:735, 1948. Julian, O. C., and Metcalf, W.: Nonobstructive Lateral Portal Vein–Vena Cava Anastomosis: Clinical Application of Smith Freeman Clamp, Arch. Surg. **59**:433 (Sept.) 1949.

made. After the removal of the clamp there was no leakage. Fifteen hundred cubic centimeters of blood was administered during the procedure.

Convalescence was uneventful, and the patient was discharged asymptomatic on the twelfth hospital day. During the period since operation she has remained asymptomatic. There has been no recurrence of either ascites or hematemesis, and she has returned to work as a waitress.

Pathological Report.—The gallbladder and a specimen of the liver were examined. Sections of the gallbladder revealed chronic cholecystitis and cholelithiasis. In the sections of the liver the architecture could not be definitely established although several areas did suggest hepatic cord cells. All sections revealed necrosis, with peripheral lymphocytic and plasma cell infiltration. There were numerous areas of extensive fibrosis with hyalinization. These sections were considered to be consistent with the clinical impression of hepar lobatum (fig 3).

COMMENT

Hepar lobatum is the result of an obliterating endarteritis in the liver producing areas of varying size of necrosis which are converted into gummas as healing takes place. Dense scare tissue is formed, and this contracts to such an extent that deep fissures are formed and the liver is divided into a series of lobes.[7]

The clinical manifestations of hepar lobatum commonly consist of ascites, pain, fever and slight jaundice. No fever or icterus was present in this patient. Hematemesis, a prominent feature in this case, was not encountered in McCrae and Caven's series of 100 cases.[8] In our patient hematemesis and ascites seemed to result from portal hypertension rather than from severe disease of the liver, since liver function tests revealed only minimal impairment. For this reason a surgical attack on the abnormal pressure relationships between the portal and caval systems appeared to be warranted.

The development of a portacaval shunt was greatly simplified by the thoracoabdominal approach, with division of the diaphragm and displacement of the liver into the chest.[9] This procedure allows for ready mobilization of the portal vein and the vena cava. The use of the Smith Freeman clamp further simplifies the procedure, since it is not necessary to dissect completely around either of the vessels but merely to expose that part of each vessel required for application of the clamp.

SUMMARY

A case of hepar lobatum is reported in which the prominent symptoms were repeated exsanguination and ascites and in which a side to side portacaval anastomosis was carried out. The advantages of the combined thoracoabdominal approach on the right and the simplification of the procedure by utilization of the Smith Freeman clamp are stressed.

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7. Boyd, W.: Pathology of Internal Diseases, ed. 4, Philadelphia, Lea & Febiger, 1944, p. 326.

8. McCrae, T., and Caven, W. R.: Tertiary Syphilis of the Liver, Am. J. M. Sc. **172**:781, 1929.

9. Satinsky, V. P.: Thoraco-Abdominal Approach for Portacaval Anastomosis, with Case Report of Portacaval Shunt Employing This Method, Ann. Surg. **128**:938, 1948.

RETROCAVAL URETER

C. ROBERT SCHMIDT, Ph.D., M.D.
D. W. HUEBERT, M.D.
AND
JAMES M. BEAZELL, Ph.D., M.D.
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Retrocaval ureter is a congenital anomaly which arises during the embryonal period when the cardinal and subcardinal veins consolidate to form the vena cava. The result is that a ureter is displaced so that, in its course to the urinary bladder, it encircles the vena cava.

While the anomaly is rare, it is becoming increasingly apparent that it is less rare than previously supposed. Pick and Anson [1] reviewed the literature in 1940, reporting 26 cases to which they added another. Of the 26 cases, only 8 were surgical and in none was the diagnosis made before operation. In four of the eight nephrectomy was performed, possibly unnecessarily, since the preoperative diagnosis was unknown. In 1948 McElhinney and Dorsey [2] reviewed the literature and reported 36 cases to which they added another diagnosed before surgical intervention, bringing the total to 37 cases. It is interesting that 10 additional cases have been added in an eight year period. Of the 37 cases, 11 were discovered at operation, and in 3 cases the diagnosis was made preoperatively, all since 1940.[3] The remaining 23 cases have been found in anatomic laboratories or at postmortem examination.

REPORT OF CASE

The patient, a white man aged 29, a welder by trade, was first seen in December 1947. The chief complaints were frequency and burning on urination, with nocturia one to two times, for the past three months, and intermittent hematuria usually in the first morning specimen for one year. He admitted to occasional backache between the shoulder blades but had not noticed any particular pain in the area of either kidney. The past history and a review of the systems were essentially noncontributory except for a weight loss of 30 pounds (13.6 Kg.) following a respiratory infection while he was in military service in the South Pacific in 1942. This weight had not been regained. In 1946 the patient had pneumonia following a submucous resection, from which he recovered completely.

Physical examination revealed a fairly well developed slender white man who appeared fatigued. The findings were not remarkable except for moderate tenderness in the area of the right kidney posteriorly. The patient was admitted to the hospital for investigation of the hematuria. A urine specimen was clear and alkaline in reaction, with a specific gravity of 1.016, 3 pus cells per high power field and no sugar albumin or red blood cells.

On cystoscopic examination there was a prominent median bar, considering the patient's age, but no evidence of a lesion to account for painless hematuria. Intravenously injected dye appeared at the left ureteral orifice in nine minutes and at the right in 14 minutes. The dye was concentrated on the left and was present only in faint traces on the right. Number 6 catheters passed readily on each side, and specimens were obtained for culture. Escherichia coli was grown in a culture from the right kidney specimen, while a culture of the left specimen was sterile.

Dr. Schmidt was formerly associate surgeon and Dr. Huebert resident surgeon, Hertzler Clinic, Halstead, Kan.

1. Pick, J. W., and Anson B. J.: Retrocaval Ureter, J. Urol. **43**:672, 1940.

2. McElhinney, P. P. B., and Dorsey, J. W.: Retrocaval Ureter, J. Urol. **59**:497, 1948.

3. Harrill, H. C.: Retrocaval Ureter, J. Urol. **44**:450, 1940. Greene, L. D., and Kearns, W. M.: Retrocaval Ureter, J. Urol. **55**:52, 1946. McElhinney and Dorsey.[2]

Retrograde pyelography revealed an entirely normal left kidney and ureter shadow. On the right side the upper third of the right ureter and the renal pelvis was markedly dilated. The lower aspect of the dilated ureter terminated in a 180 degree bend which displaced the ureter almost to the midline. The lower two thirds of the ureter appeared normal except for the displaced middle third (fig. 1). A diagnosis of extrinsic obstruction, aberrant vessel, of the right ureter with hydronephrosis was made. Surgical intervention was advised to release the obstruction.

The patient was readmitted 20 days later after a course of sulfamerazine therapy. There had been no hematuria in the interval, and laboratory data were not remarkable. A urea clearance of 72 per cent (normal) was obtained. The kidney and ureter were exposed through

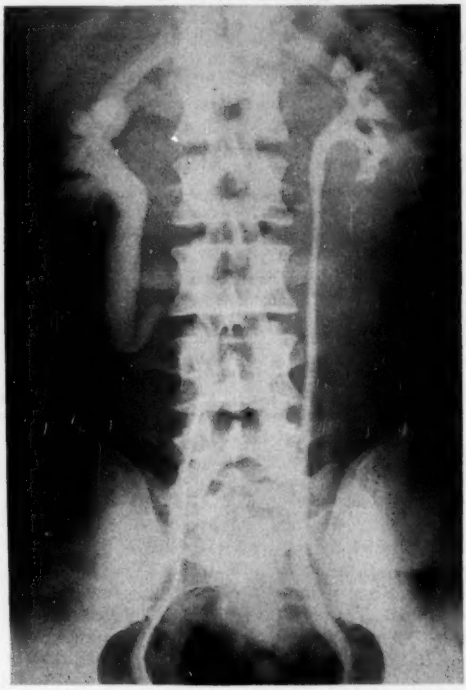

Fig. 1.—Preoperative ureteropyelogram showing medial displacement of right ureter with dilatation of renal pelvis and upper third of ureter.

a flank incision with the patient under spinal anesthesia. Grossly, the kidney appeared normal. The upper third of the ureter was dilated to the size of a thumb. Its course was medialward where it passed beneath the vena cava at the level of the third lumbar vertebra. It then passed over the medial aspect of the vena cava to pursue its course to the bladder in the usual location. From the point at which the ureter passed beneath the vena cava there was no dilatation distally.

The ureter was sectioned at the lower aspect of the dilated upper third, and the distal portion was then mobilized to its site beneath the vena cava by sharp and blunt dissection. The ureter was then brought from its postcaval location and the sectioned ends anastomosed in two layers with interrupted fine chromic and silk sutures. The site was drained with a small cigaret drain and the incision closed in layers.

The postoperative course was uneventful except for nausea, which required parenteral administration of fluids the first three days, and chills and fever (102 F.) on the second postoperative day, which responded promptly to penicillin therapy. Sulfamerazine was given for five days before the patients' dismissal on the thirteenth postoperative day.

A ureteral catheter specimen two months after operation from the right ureter yielded E. coli on culture. Retrograde pyelography at this time revealed dilatation of the upper third of the ureter and the renal pelvis but of a somewhat lesser degree than originally (fig. 2). Sulfonamide therapy was given for the pyelitis. Ureteral culture five months after operation gave negative results. The patient has been followed for two years, without recurrence of urinary symptoms.

Fig. 2.—Postoperative ureteropyelogram two months after transplantation of retrocaval ureter.

COMMENT

The incidence of retrocaval ureter is very likely greater than is generally supposed. This is supported by the fact that only 26 cases were reported in the literature up to 1940, of which only eight were discovered at operation. In contrast, during the period between 1940 and 1948, 10 additional cases were reported, of which the three additional surgical cases were diagnosed preoperatively. To the latter we add a fourth.

Retrocaval ureter with its associated hydroureteropyelonephrosis apparently produces no symptoms unless infection is superimposed. The source of intermittent hematuria in this case is obscure, unless it was associated with the existing pyelitis. In the absence of a palpable lower quadrant abdominal tumor, the roentgen findings on ureteropyelography are so characteristic (fig. 1) that an unequivocal preoperative diagnosis should be possible.

SUMMARY

A case of retrocaval ureter is presented. The chief symptoms were intermittent hematuria for one year, tenderness in the loin for several years and symptoms of cystitis for several months. Retrograde pyelography gave a characteristic picture discussed in the text and shown in the photographs.

NOTE.—Before this manuscript was accepted for publication, another case of retrocaval ureter, diagnosed preoperatively and successfully repaired surgically, was reported by Olson and Austin.[4]

1027 South Tejon.

4. Olson, R. O., and Austin, G.: Postcaval Ureter: Report and Discussion of Case with Successful Surgical Repair, New England J. Med. **242**:963, 1950.

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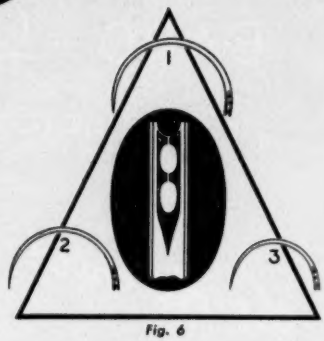

Fig. 6

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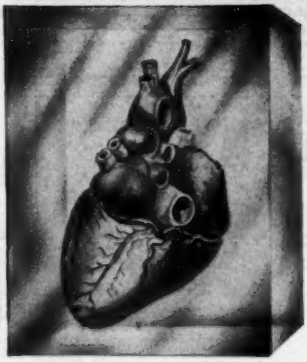

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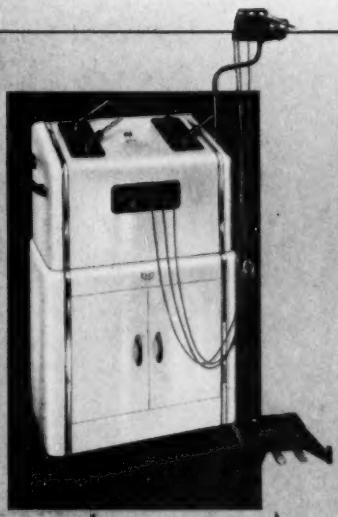

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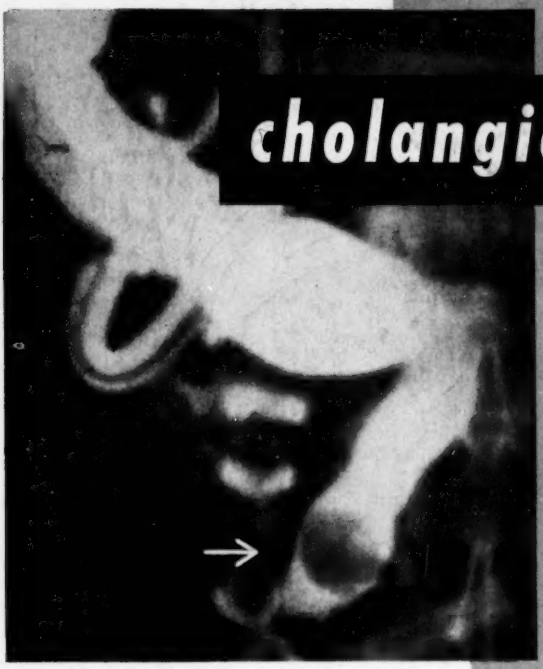

cholangiography

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"Since 1934 we have employed visualizing cholangiograms in all operations on the extrahepatic biliary system. More than 1700 studies have been made and from this experience much information has been obtained. Operative cholangiograms demonstrate congenital aberrations and anatomic displacements of the extrahepatic biliary system; determine patency of the ductal system; note number and position of offending calculi; designate functional status of the sphincter of Oddi; outline fistulous communications; visualize bile reflux into the pancreatic ducts; detect intrusions of neoplasms which impinge on the large bile ducts or originate in the ampulla of Vater; and visualize dilatation, sacculation or diverticular enlargements of the bile ducts themselves. Such exact information permits the surgeon to select the operative procedures best suited to alleviate existing pathologic abnormalities."[2]

1. Byrne, R. V.: *Amer. Jour. Surg.*, 78:514, Oct., 1949.
2. Hicken, N. F., Stevenson, U. L., Franz, B.J., Crowder, Earl: *Amer. Jour. Surg.*, 78:347, Sept., 1949.